



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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<b>(21) International Application Number:</b> <b>PCT/GB99/04377</b> <b>(22) International Filing Date:</b> <b>22 December 1999 (22.12.99)</b>  <b>(30) Priority Data:</b> <table border="0"> <tr><td>9828359.1</td><td>22 December 1998 (22.12.98)</td><td>GB</td></tr> <tr><td>9828353.4</td><td>22 December 1998 (22.12.98)</td><td>GB</td></tr> <tr><td>9828352.6</td><td>22 December 1998 (22.12.98)</td><td>GB</td></tr> <tr><td>9828355.9</td><td>22 December 1998 (22.12.98)</td><td>GB</td></tr> <tr><td>9828354.2</td><td>22 December 1998 (22.12.98)</td><td>GB</td></tr> <tr><td>9828349.2</td><td>22 December 1998 (22.12.98)</td><td>GB</td></tr> <tr><td>9828345.0</td><td>22 December 1998 (22.12.98)</td><td>GB</td></tr> <tr><td>9828350.0</td><td>22 December 1998 (22.12.98)</td><td>GB</td></tr> <tr><td>9828357.5</td><td>22 December 1998 (22.12.98)</td><td>GB</td></tr> <tr><td>9828356.7</td><td>22 December 1998 (22.12.98)</td><td>GB</td></tr> <tr><td>9900084.6</td><td>4 January 1999 (04.01.99)</td><td>GB</td></tr> <tr><td>9900082.0</td><td>4 January 1999 (04.01.99)</td><td>GB</td></tr> <tr><td>9900085.3</td><td>4 January 1999 (04.01.99)</td><td>GB</td></tr> <tr><td>9900086.1</td><td>4 January 1999 (04.01.99)</td><td>GB</td></tr> <tr><td>9900083.8</td><td>4 January 1999 (04.01.99)</td><td>GB</td></tr> <tr><td>9901916.8</td><td>28 January 1999 (28.01.99)</td><td>GB</td></tr> <tr><td>9901922.6</td><td>28 January 1999 (28.01.99)</td><td>GB</td></tr> </table>		9828359.1	22 December 1998 (22.12.98)	GB	9828353.4	22 December 1998 (22.12.98)	GB	9828352.6	22 December 1998 (22.12.98)	GB	9828355.9	22 December 1998 (22.12.98)	GB	9828354.2	22 December 1998 (22.12.98)	GB	9828349.2	22 December 1998 (22.12.98)	GB	9828345.0	22 December 1998 (22.12.98)	GB	9828350.0	22 December 1998 (22.12.98)	GB	9828357.5	22 December 1998 (22.12.98)	GB	9828356.7	22 December 1998 (22.12.98)	GB	9900084.6	4 January 1999 (04.01.99)	GB	9900082.0	4 January 1999 (04.01.99)	GB	9900085.3	4 January 1999 (04.01.99)	GB	9900086.1	4 January 1999 (04.01.99)	GB	9900083.8	4 January 1999 (04.01.99)	GB	9901916.8	28 January 1999 (28.01.99)	GB	9901922.6	28 January 1999 (28.01.99)	GB	<b>(71) Applicant (for all designated States except US):</b> MICRO-SCIENCE LIMITED [GB/GB]; 545 Eskdale Road, Winkersley Triangle, Wokingham, Berkshire RG41 5TU (GB). <b>(72) Inventors; and</b> <b>(75) Inventors/Applicants (for US only):</b> HUGHES, Martin, John, Glenton [GB/GB]; Dept. of Infectious Diseases, Imperial College School of Medicine at the Hammersmith Campus, Du Cane Road, London W12 0NN (GB). SANTANGELO, Joseph, David [GB/GB]; Dept. of Infectious Diseases, Imperial College School of Medicine at the Hammersmith Campus, Du Cane Road, London W12 0NN (GB). LANE, Jonathan, Douglas [GB/GB]; Dept. of Infectious Diseases, Imperial College School of Medicine at the Hammersmith Campus, Du Cane Road, London W12 0NN (GB). EVEREST, Paul [GB/GB]; Dept. of Infectious Diseases, Imperial College School of Medicine at the Hammersmith Campus, Du Cane Road, London W12 0NN (GB). FELDMAN, Robert [GB/GB]; Dept. of Infectious Diseases, Imperial College School of Medicine at the Hammersmith Campus, Du Cane Road, London W12 0NN (GB). MOORE, Joanne, Christine [GB/GB]; Dept. of Infectious Diseases, Imperial College School of Medicine at the Hammersmith Campus, Du Cane Road, London W12 0NN (GB). WILSON, Rebecca, Kerry [GB/GB]; ICSTM, Dept. of Biochemistry, Exhibition Road, London SW7 2AZ (GB). DOBSON, Richard, James [GB/GB]; Dept. of Infectious Diseases, Imperial College School of Medicine at the Hammersmith Campus, Du Cane Road, London W12 0NN (GB). DOUGAN, Gordon [GB/GB]; ICSTM, Dept. of Biochemistry, Exhibition Road, London SW7 2AZ (GB).  <b>(74) Agent:</b> GILL JENNINGS & EVERY; Broadgate House, 7 Eldon Street, London EC2M 7LH (GB).  <b>(81) Designated States:</b> AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>Without international search report and to be republished upon receipt of that report.</i>
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<b>(54) Title:</b> GENES AND PROTEINS, AND THEIR USE  <b>(57) Abstract</b> <p>According to the present invention, a series of genes are identified in Group B <i>Streptococcus</i>, the products of which may be associated with the outer surface of the organism. The genes, or functional fragments thereof, may be useful in the preparation of therapeutics, e.g. vaccines to immunise a patient against microbial infection.</p>																																																					

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GENES AND PROTEINS, AND THEIR USEField of the Invention

This invention relates to the identification of  
5 bacterial genes and proteins, and their use. More particularly, it relates to their use in therapy, for immunisation and in screening for drugs.

Background to the Invention

Group B *Streptococcus* (GBS), also known as  
10 *Streptococcus agalactiae*, is the causative agent of various conditions. In particular, GBS causes:

*Early onset neonatal infection.*

This infection usually begins in utero and causes severe septicaemia and pneumonia in infants, which is  
15 lethal if untreated and even with treatment is associated with a 10-20% mortality rate.

*Late onset neonatal infection.*

This infection occurs in the period shortly after birth until about 3 months of age. It causes a  
20 septicaemia, which is complicated by meningitis in 90% of cases. Other focal infections also occur including osteomyelitis, septic arthritis, abscesses and endophthalmitis.

*Adult infections.*

25 These appear to be increasingly common and occur most frequently in women who have just delivered a baby, the elderly and the immunocompromised. They are characterised by septicaemia and focal infections including osteomyelitis, septic arthritis, abscesses and  
30 endophthalmitis.

*Urinary tract infections.*

GBS is a cause of urinary tract infections and in pregnancy accounts for about 10% of all infections.

*Veterinary infections.*

35 GBS causes chronic mastitis in cows. This, in turn, leads to reduced milk production and is therefore of considerable economic importance.

GBS infections can be treated with antibiotics. However, immunisation is preferable. It is therefore desirable to develop an immunogen that could be used in a therapeutically-effective vaccine.

5 Summary of the Invention

The present invention is based on the identification of a series of genes in GBS, and also related organisms, the products of which may be localised on the outer surface of the organism and therefore may be used as a target for  
10 immuno-therapy.

According to one aspect of the invention, a peptide is encoded by an operon including any of the genes identified herein as pho1-13, pho3-21, pho2-15, pho3-18, pho3-22, pho3-3, pho3-17, pho2-2, pho1-5, pho3-1, pho3-23, pho3-50,  
15 pho1-14, pho2-10, pho3-14, pho3-24 and pho3-29, obtainable from Group B *Streptococcus*, or a homologue or functional fragment thereof. Such a peptide is suitable for therapeutic use, e.g. when isolated.

The term "functional fragments" is used herein to  
20 define a part of the gene or peptide which retains the activity of the whole gene or peptide. For example, a functional fragment of the peptide may be used as an antigenic determinant, useful in a vaccine or in the production of antibodies.

25 A gene fragment may be used to encode the active peptide. Alternatively, the gene fragment may have utility in gene therapy, targetting the wild-type gene *in vivo* to exert a therapeutic effect.

A peptide according to the present invention may  
30 comprise any of the amino acid sequences identified herein as SEQ ID NOS. 2, 4, 6, 8, 10, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33 and 35, or a functional fragment thereof.

Because of the extracellular or cell surface location,  
35 the peptides of the present invention may be suitable candidates for the production of therapeutically-effective vaccines against GBS. The term "therapeutically-effective"

is intended to include the prophylactic effect of vaccines. For example, a vaccine may comprise a peptide according to the invention, or the means for its expression, for the treatment of infection. The vaccine may be administered to females prior to or during pregnancy to protect mother and neonate against infection by GBS.

According to another aspect of the invention, the peptides or genes may be used for screening potential antimicrobial drugs or for the detection of virulence.

A further aspect of this invention is the use of any of the products identified herein, for the treatment or prevention of a condition associated with infection by a Group B Streptococcal strain.

Although the protein has been described for use in the treatment of patients, veterinary uses of the products of the invention are also considered to be within the scope of the present invention. In particular, the peptides or the vaccines may be used in the treatment of chronic mastitis, especially in cows.

#### Description of the Invention

The present invention is described with reference to Group B Streptococcal strain M732. However, all the GBS strains and many other bacterial strains are likely to include related peptides or proteins having amino acid sequence homology with the peptide of M732. Organisms likely to contain the peptides include, but are not limited to, *S. pneumoniae*, *S. pyogenes*, *S. suis*, *S. milleri*, Group C and Group G Streptococci and Enterococci. Vaccines to each of these may be developed in the same way as described for GBS.

Preferably, the peptides that may be useful for the production of vaccines have greater than 40% sequence similarity with the peptides identified herein. More preferably, the peptides have greater than 60% sequence similarity. Most preferably, the peptides have greater than 80% sequence similarity, e.g. 95% similarity.

Having characterised a gene according to the invention, it is possible to use the gene sequence to establish homologies in other microorganisms. In this way it is possible to determine whether other microorganisms have similar outer surface products. Sequence homologies may be established by searching in existing databases, e.g. EMBL or Genbank.

Peptides or proteins according to the invention may be purified and isolated by methods known in the art. In particular, having identified the gene sequence, it will be possible to use recombinant techniques to express the genes in a suitable host. Active fragments and homologues can be identified and may be useful in therapy. For example, the peptides or their active fragments may be used as antigenic determinants in a vaccine, to elicit an immune response. They may also be used in the preparation of antibodies, for passive immunisation, or diagnostic applications. Suitable antibodies include monoclonal antibodies, or fragments thereof, including single chain fv fragments. Methods for the preparation of antibodies will be apparent to those skilled in the art.

The preparation of vaccines based on attenuated microorganisms is known to those skilled in the art. Vaccine compositions can be formulated with suitable carriers or adjuvants, e.g. alum, as necessary or desired, and used in therapy, to provide effective immunisation against Group B Streptococci or other related microorganisms. The preparation of vaccine formulations will be apparent to the skilled person.

More generally, and as is well known to those skilled in the art, a suitable amount of an active component of the invention can be selected, for therapeutic use, as can suitable carriers or excipients, and routes of administration. These factors will be chosen or determined according to known criteria such as the nature/severity of the condition to be treated, the type or health of the subject etc.

The products of the present invention were identified as follows:

A partial gene library of GBS (strain M732) chromosomal DNA was prepared using the plasmid vectors pFW-phoA1, pFW-phoA2 and pFW-phoA3 (Podbielski, A. et al. 1996. Gene 177:137-147). These plasmids possess a constitutive spectinomycin adenyltransferase antibiotic resistance marker, which confers a high level of spectinomycin resistance and is therefore easily selected. Furthermore, these vectors contain a truncated (leaderless) *Escherichia coli* phoA gene for alkaline phosphatase. The three vectors differ only with respect to the reading frame in which the leaderless phoA gene exists, as compared to an upstream in-frame BamHI restriction enzyme site. Because this truncated *E. coli* phoA gene lacks the appropriate leader sequence for export of this enzyme across the bacterial membrane, extracellular alkaline phosphatase activity is absent when these plasmids are propagated in an *E. coli* phoA mutant (e.g. strain DH5 $\alpha$ ). The chromogenic alkaline phosphatase substrate, XP (5-bromo-4-chloro-3-indolyl-phosphate), does not enter intact bacterial cells and therefore only exported or surface associated alkaline phosphatase activity can be detected. When exported or surface associated alkaline phosphatase activity is present, the chromogenic XP substrate is cleaved to yield a blue pigment and the corresponding bacterial colonies can be identified by their blue colour.

Plasmid DNA was digested to completion with BamHI and dephosphorylated using shrimp alkaline phosphatase. GBS genomic DNA was partially digested with Sau3AI, size fractionated on a sucrose gradient and fragments <1kb in size were ligated into the prepared pFW-phoA vectors. *E. coli* strain DH5 $\alpha$  was chosen as the cloning host since it lacks a functional phoA gene. Recombinant plasmids were selected on Luria agar containing 100  $\mu$ g/ml of spectinomycin and 40  $\mu$ g/ml of the chromogenic XP substrate. *E. coli* transformants harbouring plasmids containing GBS

insert DNA that complements the export signal sequence of the leaderless *phoA* gene were identified by the blue colour of the colonies. Approximately 30000 different recombinant plasmids containing GBS insert DNA were screened in this manner and 83 recombinant plasmids, which complemented the leaderless *phoA*, were chosen for further study.

From these experiments, several clones were selected each containing a plasmid containing a gene (or part thereof), which complemented the leaderless *phoA*.

Having identified the gene in each clone it is then possible to obtain the full-length gene sequence, as follows.

Using the identified and sequenced gene fragment, oligonucleotide primers were designed for genomic DNA sequencing. These primers were designed so as to sequence in an 'outward' direction from the obtained sequence. Once read, the sequence obtained was checked to see if the 5' and 3' termini of the gene had been reached. The presence of these features was identified by checking against homologous sequences, and for the 5' end the presence of an AUG start codon (or accepted equivalent) preceded by a Shine-Dalgarno consensus sequence, and for the 3' end, the presence of a translation termination (Stop) codon.

Upon identification of the full-length gene, primers were designed for amplification of full-length product. Primers used included restriction enzyme recognition sites (NcoI at the 5' end and EcoO109I at the 3' end) to allow subsequent cloning of the product into the Lactococcal expression system used.

PCR was carried out using the primers, and the products cloned into a pCR 2.1 cloning vector (In Vitrogen). Following confirmation of the presence of the cloned fragment, the DNA was excised using the restriction enzymes NcoI and EcoO109I.

The vector into which this fragment was inserted was a modified version of pNZ8048 (Kuipers, O. P. et al. (1998) J. Biotech 64: 15-21). This vector, harbouring a



lactococcal origin of replication, a chloramphenicol resistance marker, an inducible nisin promoter and a multicloning site was altered by the replacement of the multicloning site with two 10X His tags, flanked on the 5-  
5 most end with an NcoI site, split in the middle with a multicloning site (including an EcoO109I site), and a Stop (termination) codon at the 3'end of the His tags.

The gene of interest was inserted so that a 10X His tag was in the 3' position relative to the coding region.  
10 Following transformation of the recombinant plasmid into *L.lactis* (strain NZ9000 - Kuipers, O. P. et al. (1998) *supra*), a 400 ml liquid culture was set up and translation of the protein was induced by the addition of nisin to the culture. After a 2 hour incubation, the cells were  
15 harvested and lysed by bead beating. The resultant lysate was cleared by centrifugation, then passed over a metal affinity (Talon, Clontech) column. The column was washed repeatedly before bound proteins were eluted with Imidazole.

20 To identify fractions containing the His-tagged recombinant protein, an aliquot from each fraction was analysed by SDS-PAGE, Western blotted and probed with anti-His antibodies.

The recombinant protein obtained was then used to  
25 immunise New Zealand white rabbits, with pre-immune sera being harvested prior to immunisation. Following a boost, the rabbits were sacrificed and sera collected. This sera was used in Western blots, ELISA and animal protection models.

30 Using the sera obtained from the animal studies, immunosorption studies were carried out.

Group B *Streptococcus* was grown in 20ml Todd Hewitt broth (THB) for 8 hours, harvested and resuspended in 5ml PBS. 50 $\mu$ l aliquots of this were used to coat wells in a 96  
35 well plate (Nunc Immuno-Sorb). This was left at 4°C overnight to allow for adsorbance of the bacteria onto the plate. Plates were washed twice with PBS, then blocked

with 3%BSA in PBS for 1hr at 37°C. Plates were again washed. Serial 10 fold dilutions of the sera were made in PBS and 50µl of these dilutions were added to the wells of the plate, in duplicate. The plate was covered and  
5 incubated for 1 hr at 37°C. The plate was washed, then 50µl anti-rabbit alkaline phosphatase conjugated secondary antibody at a concentration of 1:5000 was added to each well. Following incubation at 37°C for an hour, the plate was washed again. 50µl substrate (PNPP) was added to each  
10 well, and the reaction allowed to proceed for 30min before the adsorbance was read at 405 nm.

Animal protection studies were also carried out to test the effectiveness of protection on the immunised rabbits.

15 GBS M732 was grown up in THB until mid-log phase was reached - approximately 5 hours. Cells were counted in a counting chamber, and bacteria were diluted to give a concentration of  $2 \times 10^7$  bacteria per ml in pre-immune or test sera. 50µl of this was injected via the  
20 intraperitoneal route into 0-1 day old mice. The mice were observed for survival over 48 hours.

The following Examples illustrate the invention.

#### Example 1

25 A first clone contained a gene sequence identified herein as SEQ ID NO. 1, with an amino acid sequence identified as SEQ ID NO. 2, and classified as pho1-13.

A comparison of the amino acid sequence of pho1-13 was performed.

30 Homologues to the GBS pho1-13 gene product can be identified in *Streptococcus pyogenes*, *S. pneumoniae*, *S. salivarius*, *Escherichia coli*, *Yersinia enterocolitica*, *Aquifex aeolicus*, *Helicobacter pylori* and *Haemophilus influenzae*. The *S. pyogenes* and *S. pneumoniae* homologues  
35 were identified from genome sequence data and no annotations were available as to the identity of the gene or gene products. In all other cases, the above homologues

can be identified as ATP-dependent Clp protease proteolytic subunits. The catalytic activity of Clp proteases results in the hydrolysis of proteins to small peptides in the presence of ATP and magnesium (Giffard, P.M. et al. 1993. J. Gen. Microbiol. 139:913-920). Furthermore, the ClpP component of Clp proteases has been shown to be induced as part of the heat shock response (Kroh, H.E. and L.D. Simon. 1990. J. Bacteriol. 172:6026-6034) and it is probable that this subunit or the complete proteolytic domain would associated with the bacterial surface.

Immunisation studies, carried out as described above, yielded the following results.

Treatment	No animals	No animals surviving	
		at time (hrs)	
		24	48
PBS	10	7	0
Pre-immunised	37	13	0
Immunised	38	17	9

#### Example 2

A second clone was selected containing a plasmid designated pho1-14. This plasmid contained a gene (or part thereof), which complemented the leaderless *phoA*. The nucleotide and deduced amino acid sequences are shown as SEQ ID NOS. 3 and 4, respectively.

A comparison of the amino acid sequence of pho1-14 was performed.

Homologues to the GBS pho1-14 gene product can be identified in *Streptococcus pyogenes*, *Enterococcus faecalis* and *Streptococcus pneumoniae*. These homologues were identified from genome sequence data and no annotations were available as to the identity of the gene or gene products. Additionally, two possible homologues were also

identified from *Shigella flexneri* (SpaR) and *Yersinia pseudotuberculosis* (YscT). These latter two homologues are related proteins, believed to be anchored in the bacterial membrane (Bergman, T. et al. 1994. J. Bacteriol. 176:2619-2626). In *S. flexneri*, the product of the *spaR* gene has been shown to be important for invasion of epithelial cells (Sasakawa, C. et al. 1993. J. Bacteriol. 175:2334-2346). Furthermore, the product of the *spaR* gene is also required for surface presentation of invasion plasmid antigens. The analogous protein in *Y. pseudotuberculosis* is a component of the Yop secretion system and is also important for virulence in this organism.

#### Example 3

A third clone was selected containing a plasmid designated pho1-5. This plasmid contained a gene (or part thereof), which complemented the leaderless *phoA*. The nucleotide and deduced amino acid sequences are shown as SEQ ID NOS. 5 and 6.

A comparison of the amino acid sequence of pho1-5 was performed.

Homologues to the GBS pho1-5 gene product can only be identified in *Streptococcus pyogenes* and *Staphylococcus carnosus* (*sceA*). The *S. pyogenes* homologue was identified from genome sequence data and no annotations were available as to the identity of the gene or gene products. Furthermore, little information is available on the function of the *sceA* gene product from *S. carnosus*. The *sceA* gene product shows some sequence similarity to the aggregation promoting protein from *Lactobacillus gasseri*. Based on analysis of the *sceA* gene product, this molecule contains a well-conserved signal sequence and is apparently secreted or associated with the bacterial cell surface.

#### Example 4

A further clone was selected containing a plasmid designated pho3-3. This plasmid contained a gene (or part thereof), which complemented the leaderless *phoA*. The

nucleotide and deduced amino acid sequences are shown as SEQ ID NOS. 7 and 8.

A comparison of the amino acid sequence of pho3-3 was performed.

5 Homologues to the GBS pho3-3 gene product can be identified in *Streptococcus mutans* (rmlC), (cpsM) *S. pneumoniae* and *S. pyogenes*. The *S. pyogenes* homologue was identified from genome sequence data and no annotations were available as to the identity of the gene or gene  
10 product. In *S. pneumoniae*, the homologue can be identified as dTDP-4-keto-6-deoxy glucose-3,5-epimerase. In the other two cases, the above homologues can be identified as dTDP-4-keto-L-rhamnose reductase (rmlC). In *S. mutans*, the gene encoding this enzyme, *rmlC*, is part of the *rml* locus.  
15 The *rml* locus consists of three genes which exhibit significant similarity to enzymes involved in the biosynthesis of dTDP-rhamnose, the immediate precursor of the rhamnose component in the *S. mutans* polysaccharide capsule (Tsukioka, Y. et al. 1997. J. Bacteriol. 179:1126-  
20 1134). An analogous locus has also been identified in *S. pneumoniae* (Coffey, T.J. et al. 1998. Mol. Microbiol. 17:73-83). Almost all *Streptococci* characteristically possess rhamnose in their cell wall associated polysaccharides (Schleifer, K.H. and R. Kilper-Bälz. 1987. Syst. Appl.  
25 Microbiol. 10:1-19), and it is highly probable that dTDP-4-keto-L-rhamnose reductase would be associated with the outer surface in *Streptococci*.

#### Example 5

A further clone was selected containing a plasmid  
30 designated pho2-10. This plasmid contained a gene (or part thereof), which complemented the leaderless *phoA*.

The nucleotide sequence is shown as SEQ ID NO. 9. From this, upstream and downstream coding regions were identified, and the deduced amino acid sequences shown as  
35 SEQ ID NOS. 10 and 11.

A comparison of the amino acid sequences of pho2-10 was performed.

Homologues to the GBS pho2-10 gene product can be identified in *Streptococcus pyogenes*, *Enterococcus faecalis*, *Debaryomyces occidentalis* (hatI) and *Escherichia coli* (trkD). The *S. pyogenes* and *E. faecalis* homologues were identified from genome sequence data and no annotations were available as to the identity of the gene or gene products. In the yeast *D. occidentalis*, the *hak1* gene is a homologue of the *trkD* gene from *E. coli* (Banuelos, M.A. et al. 1995. EMBO J. 14:3021-3027). The *trkD* gene of *E. coli* is part of the *kup* potassium uptake system. The specific homolog identified here is the *kup* system potassium uptake protein. The *kup* system is a constitutive potassium uptake system in *E. coli*. The *kup* system potassium uptake protein contains a highly hydrophobic N-terminus that is predicted to span the membrane at least 12 times. *Kup* is not homologous to other known membrane protein sequences. There is no indication of ATP binding, and it is proposed that the system is driven by a chemiosmotic gradient (Schleyer, M. & E.P. Bakker, 1993. J. Bacteriol. 175:6925-6931).

#### Example 6

A further clone was selected containing a plasmid designated pho2-15. This plasmid contained a gene (or part thereof), which complemented the leaderless *phoA*. The nucleotide and deduced amino acid sequences of the gene are shown as SEQ ID NOS. 12 and 13.

A comparison of the amino acid sequence of pho2-15 was performed.

Homologues to the GBS pho2-15 gene product can be identified in *Streptococcus pyogenes*, *Streptococcus pneumoniae*, *Enterococcus faecalis* and *Escherichia coli* (*gatC* and *SgcC*). The *S. pyogenes*, *S. pneumoniae* and *E. faecalis* homologues were identified from genome sequence data and no annotations were available as to the identity of the gene or gene products. In *E. coli*, the *gatC* and *sgcC* gene products can be identified as being the IIC component of phosphoenolpyruvate-dependent sugar

phosphotransferase systems (PTS), a major carbohydrate active-transport system. In PTS systems, the IIC component is typically involved in binding of extracellular carbohydrates and forms a complex with the IID component to constitute a membrane channel (Nobelmann, B. and J.W. Lengeler. 1995. Biochim. Biophys. Acta 1262:69-72).

#### Example 7

A further clone was selected containing a plasmid designated pho2-2. This plasmid contained a gene (or part thereof), which complemented the leaderless *phoA*. The nucleotide and deduced amino acid sequences of the gene are shown as SEQ ID NOS. 14 and 15, respectively.

A comparison of the amino acid sequence of pho2-2 was performed.

Homologues to the GBS pho2-2 gene product can be identified in *Enterococcus faecalis*, *Escherichia coli* (malk and afuC), *Bacillus subtilis* (glnO), *Haemophilus influenzae* (yebM and potA), *Streptococcus pyogenes*, *Streptococcus pneumoniae* and *Salmonella typhimurium* (malk). The *E. faecalis*, *S. pyogenes* and *S. pneumoniae* homologues were identified from genome sequence data and no annotations were available as to the identity of the gene or gene products. In all other cases, homologues represented ATP-binding transport proteins that are part of ABC type transporters. Many of the components of ABC type transporters are membrane or cell surface associated, as these systems are involved in the transport of macromolecules from the extracellular environment to the intracellular compartment.

#### Example 8

A further clone was selected containing a plasmid designated pho3-14. This plasmid contained a gene (or part thereof), which complemented the leaderless *phoA*. The nucleotide and deduced amino acid sequences of the gene are shown as SEQ ID NOS. 16 and 17.

A comparison of the amino acid sequence of pho3-14 was performed and no homologues could be identified in any of

the public databases. One homologue to the GBS pho3-14 gene product can be identified in *Streptococcus pyogenes*, but this homologue was identified from genome sequence data and no annotations were available as to the identity of the gene or gene product. Using this *S. pyogenes* homologue to search the public databases yielded no further information. Since the pho3-14 product complemented the leaderless *phoA* gene, it can be concluded that this protein (or part thereof) would most probably be located extracellularly.

#### 10 Example 9

A further clone was selected containing a plasmid designated pho3-17. This plasmid contained a gene (or part thereof), which complemented the leaderless *phoA*. The nucleotide and deduced amino acid sequences of the gene are shown as SEQ ID NOS. 18 and 19.

A comparison of the amino acid sequence of pho3-17 was performed.

Homologues to the GBS Pho3-17 gene product can be identified in *Streptococcus mutans* and *Lactococcus lactis*, with similarity being shown to N-acetyl muramidase. Similarity is also seen with an unidentified gene, *yubE* from *Bacillus subtilis*.

N-acetylmuramidase is an autolysin that is involved in cell division. Using this limited information along with the fact that pho3-17 complemented the leaderless *phoA* gene, it can be concluded that the pho3-17 product would most probably be located extracellularly.

#### Example 10

A further clone was selected containing a plasmid designated pho3-18. This plasmid contained a gene (or part thereof), which complemented the leaderless *phoA*. The nucleotide and deduced amino acid sequences of the gene are shown as SEQ ID NOS. 20 and 21.

A comparison of the amino acid sequence of pho3-18 was performed.

Homologues to the GBS pho3-18 gene product can be identified in *Streptococcus pyogenes* and *Streptococcus*



*pneumoniae*. These homologues were identified from genome sequence data and no annotations were available as to the identity of the gene or gene products. Using these *S. pyogenes* and *S. pneumoniae* homologues to search the public databases showed some similarity to outer surface and membrane spanning proteins. Since the ORF3-18 product complemented the leaderless *phoA* gene, it can be concluded that this protein (or part thereof) would most probably be located extracellularly.

10 Example 11

A further clone was selected containing a plasmid designated *pho3-1*. This plasmid contained a gene (or part thereof), which complemented the leaderless *phoA*. The nucleotide and deduced amino acid sequences of the gene are shown as SEQ ID NOS. 22 and 23.

A comparison of the amino acid sequence of *pho3-1* was performed.

Homologues to the GBS *pho3-1* gene product can be identified in *Streptococcus pyogenes*, *Streptococcus pneumoniae*, *Bacillus subtilis* (*yutD*) and *Enterococcus faecalis*. The *S. pyogenes*, *S. pneumoniae* and *E. faecalis* homologues were identified from genome sequence data and no annotations were available as to the identity of the gene or gene products. In *B. subtilis*, the function of the *yutD* gene product is unknown. It can be noted however, that the *yutD* gene is located on the *B. subtilis* chromosome in a region containing genes involved in cell wall synthesis. The fact that this DNA sequence complemented the leaderless *phoA* gene suggests that this gene product is extracellularly located.

30 Example 12

A further clone was selected containing a plasmid designated *pho3-21*. This plasmid contained a gene (or part thereof), which complemented the leaderless *phoA*. The nucleotide and deduced amino acid sequences of the gene are shown as SEQ ID NOS. 24 and 25.

A comparison of the amino acid sequence of pho3-21 was performed.

Homologues to the GBS pho3-21 gene product can be identified in *Streptococcus pyogenes*, *Streptococcus pneumoniae*, *Lactobacillus fermentum* (bspA) and *Lactobacillus reuteri* (cnb). The *S. pyogenes* and *S. pneumoniae* homologues were identified from genome sequence data and no annotations were available as to the identity of the gene or gene products. In *L. fermentum*, the bspA gene product has been identified as being a basic cell surface-located protein that has some sequence similarity to family III of the bacterial solute-binding proteins (Turner, M.S. et al. 1997. J. Bacteriol. 179:3310-3316). In *L. reuteri*, the cnb gene product has been identified as a collagen binding protein that has some sequence similarity to the solute-binding component of bacterial ABC transporters (Roos, S. et al. 1996. FEMS Microbiol. Lett. 144:33-38).

#### Example 13

A further clone was selected containing a plasmid designated pho3-22. This plasmid contained a gene (or part thereof), which complemented the leaderless phoA. The nucleotide and deduced amino acid sequences of the gene are shown as SEQ ID NOS. 26 and 27.

A comparison of the amino acid sequence of pho3-22 was performed.

Homologues to the GBS pho3-22 gene product can be identified in *Enterococcus faecalis*, *Streptococcus equisimilis* (lppC), *Pseudomonas fluorescens* (oprI) and *Streptococcus thermophilus* (orf142). The *E. faecalis* homolog was identified from genome sequence data and no annotations were available as to the identity of the gene or gene products. In *S. equisimilis*, the lppC gene product has been identified as being a lipoprotein that is homologous to the E(P4) outer membrane protein from *Haemophilus influenzae* (Gase, K. et al. 1997. Med. Microbiol. Immunol. 186:63-73). Likewise, the P.

*fluorescens* *oprI* gene encodes a major outer membrane lipoprotein (Cornelis, P. et al. 1989. Mol. Microbiol. 3:421-428). In *S. thermophilus*, the *orf142* product has been putatively identified as a cell surface exposed lipoprotein that may act as a receptor for the bacteriophages TP-J34 and Sfi21 (Neve, H. et al. 1998. Virology 241:61-72). The ORF3-22 product showed good similarity to the above homologues, particularly at the N-terminus. This is most likely the region required for complementation of the leaderless *phoA* gene, and therefore serves as a leader sequence.

#### Example 14

A further clone was selected containing a plasmid designated *pho3-23*. This plasmid contained a gene (or part thereof), which complemented the leaderless *phoA*. The nucleotide and deduced amino acid sequences of the genes are shown as SEQ ID NOS. 28 and 29.

A comparison of the amino acid sequence of *pho3-23* was performed.

Homologues to the GBS *pho3-23* gene product can be identified in *Streptococcus pyogenes*, *Streptococcus pneumoniae*, *Enterococcus faecalis* and *Streptococcus mutans* (*perM*). The *S. pyogenes*, *S. pneumoniae* and *E. faecalis* homologues were identified from genome sequence data and no annotations were available as to the identity of the gene or gene products. In *S. mutans*, the *perM* gene product has been presumptively identified as a permease, but no other information is available as to the function of this protein. Considering that the *pho3-23* coding region complements the leaderless *phoA* gene, it can be concluded that the *pho3-17* gene product would most probably be located extracellularly.

#### Example 15

A further clone was selected containing a plasmid designated *pho3-24*. This plasmid contained a gene (or part thereof), which complemented the leaderless *phoA*. The

nucleotide and deduced amino acid sequences of the gene are shown as SEQ ID NOS. 30 and 31.

A comparison of the amino acid sequence of pho3-24 was performed.

5 Homologues to the GBS pho3-24 gene product can be identified in *Streptococcus mutans* (dltB), *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Enterococcus faecalis*, *Lactobacillus casei* (dltB) and *Bacillus subtilis* (dltB). The *S. pneumoniae*, *S. pyogenes* and *E. faecalis* homologues  
10 were identified from genome sequence data and no annotations were available as to the identity of the gene or gene products. In *S. mutans*, *L. casei* and *B. subtilis*, the dltB gene product has been identified as being a basic membrane protein that is involved in the transport of  
15 activated D-alanine through the cell membrane. The dltB gene product is involved in the biosynthesis of D-alanyl-lipoteichoic acid (Heaton, M.P. and F.C. Neuhaus. 1992. J. Bacteriol. 174:4707-4717). In *L. casei* and *B. subtilis*, the dltB gene product is believed to contain at least 9  
20 membrane spanning domains, indicating that the protein or portions thereof are exposed to the outside of the cell.

#### Example 16

A further clone was selected containing a plasmid designated pho3-29. This plasmid contained a gene (or part  
25 thereof), which complemented the leaderless phoA. The nucleotide and deduced amino acid sequences of the gene are shown as SEQ ID NOS. 32 and 33.

A comparison of the amino acid sequence of pho3-29 was performed.

30 Homologues to the GBS pho3-29 gene product can be identified in *Borrelia burgdorferi* (p23 or ospC), *Bacillus brevis* (owp) and *Pseudomonas aeruginosa* (oprI). Although these homologues are not related to each other, they all represent major outer surface proteins. In *B. burgdorferi*,  
35 the ospC gene product has been identified as being a 23-kDa protein that is the immunodominant antigen on the surface of this bacterium (Padula, S.J. et al. 1993. Infect. Immun.

61:5097-5105). The *owp* gene product from *B. brevis* is one of two major cell wall proteins involved in the surface layer lattice (Tsuboi, A. 1988. J. Bacteriol. 170:935-945). Finally, the *oprI* gene from *P. aeruginosa* encodes a major outer membrane lipoprotein precursor (Saint-Onge, A. et al. 1992. J. Gen. Microbiol. 138:733-741).

Example 17

A further clone was selected containing a plasmid designated pho3-50. This plasmid contained a gene (or part thereof), which complemented the leaderless *phoA*. The nucleotide and deduced amino acid sequences of the gene are shown as SEQ ID NOS. 34 and 35.

A comparison of the amino acid sequence of pho3-50 was performed.

Homologues to the GBS pho3-50 gene product can be identified in a variety of Streptococci (*penA*, *pbp2B*, *pbpB2*), *Borrelia burgdorferi* (*pbp2*), *Enterococcus faecalis* (*pbpC*), *Staphylococcus aureus* (*pbpA*), *Mycobacterium leprae* (*pbpB*) and *Helicobacter pylori* (*pbp2*). In all cases, the above homologues can be identified as penicillin binding proteins (PBPs). Genes encoding penicillin binding proteins are often located in a cluster of genes associated with cell wall synthesis (Pucci, M.J. et al. 1997. J. Bacteriol. 179:5632-5635). Furthermore, PBPs are typically integrated into the cell wall of a bacterium with some or all of the protein being exposed on the outer bacterial surface.

CLAIMS

1. A peptide encoded by an operon including any of the genes identified herein as pho1-13, pho3-21, pho2-15, pho3-18, pho3-22, pho3-3, pho3-17, pho2-2, pho1-5, pho3-1, pho3-23, pho3-50, pho1-14, pho2-10, pho3-14, pho3-24 and pho3-29, obtainable from Group B *Streptococcus*, or a homologue thereof or a functional fragment thereof.
2. A peptide according to claim 1, comprising any of the amino acid sequences identified herein as SEQ ID NOS. 2, 4, 6, 8, 10, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33 and 35.
3. A peptide according to claim 1 or claim 2, for therapeutic use.
4. A polynucleotide encoding a peptide according to claim 1 or claim 2, for therapeutic use.
5. A host transformed to express a peptide according to claim 1 or claim 2.
6. A vaccine comprising a peptide according to claim 1 or claim 2, or the means for its expression.
7. Use of a product according to any of claims 1 to 5, for screening potential drugs or for the detection of virulence.
8. Use of a product according to any of claims 1 to 5, for the manufacture of a medicament for use in the treatment or prevention of a condition associated with bacterial infection.
9. Use according to claim 8, wherein the infection is a Group B streptococcal infection.
10. Use according to claim 8 or claim 9, wherein the infection is a focal infection.
11. Use according to claim 8 or claim 9, wherein the infection is a urinary tract infection.
12. An antibody raised against a peptide according to claim 1 or claim 2.

## SEQUENCE LISTING

&lt;110&gt; Microscience Limited

&lt;120&gt; GENES AND PROTEINS, AND THEIR USE

&lt;130&gt; REP05973WO

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 50 55 60

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 Ser Phe Thr Lys Lys Asn Thr Leu Arg Gly Leu His Ala Glu Pro Trp  
 65 70 75 80

gat aaa tat gtt tcg atc gct gat gaa gga cgt gtg atc ggt act tgg 288  
 Asp Lys Tyr Val Ser Ile Ala Asp Glu Gly Arg Val Ile Gly Thr Trp  
 85 90 95

gtt gac ctc cgt gaa ggt gac agt ttt ggt aac gtt tac caa acg att 336  
 Val Asp Leu Arg Glu Gly Asp Ser Phe Gly Asn Val Tyr Gln Thr Ile  
                   100                                  105                                  110

atc gat gcc tca aaa ggt att ttt gtt cca cgc ggc gtt gct aat ggt 384  
 Ile Asp Ala Ser Lys Gly Ile Phe Val Pro Arg Gly Val Ala Asn Gly  
                   115                                  120                                  125

ttc caa gtt ctt tca gat aaa gca gct tat act tat ctc gtt aac gat 432  
 Phe Gln Val Leu Ser Asp Lys Ala Ala Tyr Thr Tyr Leu Val Asn Asp  
                   130                                  135                                  140

tat tgg gca ctt gaa ctc aaa cca aaa tat gct ttc gtt aac tat gca 480  
 Tyr Trp Ala Leu Glu Leu Lys Pro Lys Tyr Ala Phe Val Asn Tyr Ala  
                   145                                  150                                  155                                  160

gat cca aat cta ggc att cag tgg gaa aat ctw gaa gaa gca gaa gtc 528  
 Asp Pro Asn Leu Gly Ile Gln Trp Glu Asn Xaa Glu Glu Ala Glu Val  
                                   165                                  170                                  175

tca gaa gca gat aag aat cac cca ctt ctc aaa gat gta aaa cct ttg 576  
 Ser Glu Ala Asp Lys Asn His Pro Leu Leu Lys Asp Val Lys Pro Leu  
                                   180                                  185                                  190

aag aag gaa gat ttg taa 594  
 Lys Lys Glu Asp Leu  
                   195

<210> 8

<211> 197

<212> PRT

<213> group B streptococcus

<400> 8

Met Thr Glu Pro Phe Phe Asp Lys Glu Leu Thr Cys Arg Pro Ile Glu  
                   1                                  5                                  10                                  15

Ala Ile Pro Glu Leu Leu Glu Phe Asp Ile Thr Val Arg Gly Asp Asn  
                   20                                  25                                  30

Arg Gly Trp Phe Lys Glu Asn Phe Gln Lys Glu Lys Met Ile Pro Leu  
                   35                                  40                                  45

Gly Phe Pro Glu Ser Phe Phe Glu Ala Asp Lys Leu Gln Asn Asn Ile  
                   50                                  55                                  60

Ser Phe Thr Lys Lys Asn Thr Leu Arg Gly Leu His Ala Glu Pro Trp

65                                      70                                      75                                      80  
 Asp Lys Tyr Val Ser Ile Ala Asp Glu Gly Arg Val Ile Gly Thr Trp  
                                     85                                      90                                      95  
 Val Asp Leu Arg Glu Gly Asp Ser Phe Gly Asn Val Tyr Gln Thr Ile  
                                     100                                      105                                      110  
 Ile Asp Ala Ser Lys Gly Ile Phe Val Pro Arg Gly Val Ala Asn Gly  
                                     115                                      120                                      125  
 Phe Gln Val Leu Ser Asp Lys Ala Ala Tyr Thr Tyr Leu Val Asn Asp  
                                     130                                      135                                      140  
 Tyr Trp Ala Leu Glu Leu Lys Pro Lys Tyr Ala Phe Val Asn Tyr Ala  
                                     145                                      150                                      155                                      160  
 Asp Pro Asn Leu Gly Ile Gln Trp Glu Asn Xaa Glu Glu Ala Glu Val  
                                     165                                      170                                      175  
 Ser Glu Ala Asp Lys Asn His Pro Leu Leu Lys Asp Val Lys Pro Leu  
                                     180                                      185                                      190  
 Lys Lys Glu Asp Leu  
                                     195

<210> 9  
 <211> 1217  
 <212> DNA  
 <213> group B streptococcus

<220>  
 <221> CDS  
 <222> (1)..(570)

<220>  
 <221> CDS  
 <222> (679)..(945)

<400> 9  
 tat tat tta atc gga ggg ttg gca gaa atg caa cat gtc aat cat tct    48  
 Tyr Tyr Leu Ile Gly Gly Leu Ala Glu Met Gln His Val Asn His Ser  
       1                                      5                                      10                                      15  
 tct ttt gat aaa gca tca aaa gca gga ttt att att gct tta ggc att    96  
 Ser Phe Asp Lys Ala Ser Lys Ala Gly Phe Ile Ile Ala Leu Gly Ile

20	25	30	
ggt tat gga gat att ggt aca agc cca ctc tat acg atg caa tca ttg			144
Val Tyr Gly Asp Ile Gly Thr Ser Pro Leu Tyr Thr Met Gln Ser Leu			
35	40	45	
ggt gaa aac caa ggt ggt att tct agt gtc aca gaa tcg ttt atc tta			192
Val Glu Asn Gln Gly Gly Ile Ser Ser Val Thr Glu Ser Phe Ile Leu			
50	55	60	
ggt tct ata tct tta atc ata tgg acc ttg aca ctt att aca act atc			240
Gly Ser Ile Ser Leu Ile Ile Trp Thr Leu Thr Leu Ile Thr Thr Ile			
65	70	75	80
aag tat gtg ctt gta gct tta aag gcg gat aat cac cac gaa ggt ggt			288
Lys Tyr Val Leu Val Ala Leu Lys Ala Asp Asn His His Glu Gly Gly			
85	90	95	
att ttt tct tta tat acc ctt gtt aga aaa atg aca cct tgg tta att			336
Ile Phe Ser Leu Tyr Thr Leu Val Arg Lys Met Thr Pro Trp Leu Ile			
100	105	110	
ggt ccg gct gtt att gga ggt gca acc ttg ttg tca gat gga gct ttg			384
Val Pro Ala Val Ile Gly Gly Ala Thr Leu Leu Ser Asp Gly Ala Leu			
115	120	125	
acg cca gct gta acc gta ctt cag ccg tta agg att aaa gta gtt cct			432
Thr Pro Ala Val Thr Val Leu Gln Pro Leu Arg Ile Lys Val Val Pro			
130	135	140	
agt ttg cag cat att tcc aga atc aga gta tgt tat ttt gcg acc ttg			480
Ser Leu Gln His Ile Ser Arg Ile Arg Val Cys Tyr Phe Ala Thr Leu			
145	150	155	160
tta ttt act gtt act ttt gcc atc caa ggt ttg gaa cgg gtg tta ttg			528
Leu Phe Thr Val Thr Phe Ala Ile Gln Gly Leu Glu Arg Val Leu Leu			
165	170	175	
gaa tta ttg gcc att atg tta tat ggt ttg cct ttt ggt tta			570
Glu Leu Leu Ala Ile Met Leu Tyr Gly Leu Pro Phe Gly Leu			
180	185	190	
ncggtctcct tatagttttg cccatccaga agttttcaag cattaatcca tactacggtt			630
tgaaattggtt atttagtcca gagaatcata aaggtatttt tatatttag gat cta ttt			687
			Asp Leu Phe
tcc tgg cga caa acg gga gca gaa gca cta tac tct gac tta ggt cat			735



Ser Trp Arg Gln Thr Gly Ala Glu Ala Leu Tyr Ser Asp Leu Gly His  
 195 200 205

gtt ggg cgt gga aat ata cat gtt tca tgg ccg ttc gtt aag gtt gcc 783  
 Val Gly Arg Gly Asn Ile His Val Ser Trp Pro Phe Val Lys Val Ala  
 210 215 220 225

att ata ctt tct tat tgt ggg caa ggg gca tgg att tta gct aat aag 831  
 Ile Ile Leu Ser Tyr Cys Gly Gln Gly Ala Trp Ile Leu Ala Asn Lys  
 230 235 240

aac gca gga aat gaa ttg aat ccc ttt ttt gct agt att cct tcg caa 879  
 Asn Ala Gly Asn Glu Leu Asn Pro Phe Phe Ala Ser Ile Pro Ser Gln  
 245 250 255

ttt aca atg cat gtc gtt att tta gct act ttg gca gct atc atc gct 927  
 Phe Thr Met His Val Val Ile Leu Ala Thr Leu Ala Ala Ile Ile Ala  
 260 265 270

tca cag gca ctg att tct ggatcaatctt accttaagtt ctgagctatg 975  
 Ser Gln Ala Leu Ile Ser  
 275

cgactaaaaa tattcccaca atttcgttca acttatcctg ttgacaatat tgggtcaaac 1035

ctacatacct ggtattaatt gggtcttatt tgccattaca acctctattg gtttgctttt 1095

taagacttca gcgcacatgg aagcagcata tggattagcg ataacaatta cgatgcta 1155

gacaactatt ttactgtctt tctttttaat tcaaaaagga gtaaagagag gttttagcta 1215

tt 1217

&lt;210&gt; 10

&lt;211&gt; 190

&lt;212&gt; PRT

&lt;213&gt; group B streptococcus

&lt;400&gt; 10

Tyr Tyr Leu Ile Gly Gly Leu Ala Glu Met Gln His Val Asn His Ser  
 1 5 10 15

Ser Phe Asp Lys Ala Ser Lys Ala Gly Phe Ile Ile Ala Leu Gly Ile  
 20 25 30

Val Tyr Gly Asp Ile Gly Thr Ser Pro Leu Tyr Thr Met Gln Ser Leu  
 35 40 45

Val Glu Asn Gln Gly Gly Ile Ser Ser Val Thr Glu Ser Phe Ile Leu  
 50 55 60  
 Gly Ser Ile Ser Leu Ile Ile Trp Thr Leu Thr Leu Ile Thr Thr Ile  
 65 70 75 80  
 Lys Tyr Val Leu Val Ala Leu Lys Ala Asp Asn His His Glu Gly Gly  
 85 90 95  
 Ile Phe Ser Leu Tyr Thr Leu Val Arg Lys Met Thr Pro Trp Leu Ile  
 100 105 110  
 Val Pro Ala Val Ile Gly Gly Ala Thr Leu Leu Ser Asp Gly Ala Leu  
 115 120 125  
 Thr Pro Ala Val Thr Val Leu Gln Pro Leu Arg Ile Lys Val Val Pro  
 130 135 140  
 Ser Leu Gln His Ile Ser Arg Ile Arg Val Cys Tyr Phe Ala Thr Leu  
 145 150 155 160  
 Leu Phe Thr Val Thr Phe Ala Ile Gln Gly Leu Glu Arg Val Leu Leu  
 165 170 175  
 Glu Leu Leu Ala Ile Met Leu Tyr Gly Leu Pro Phe Gly Leu  
 180 185 190

&lt;210&gt; 11

&lt;211&gt; 89

&lt;212&gt; PRT

&lt;213&gt; group B streptococcus

&lt;400&gt; 11

Asp Leu Phe Ser Trp Arg Gln Thr Gly Ala Glu Ala Leu Tyr Ser Asp  
 1 5 10 15  
 Leu Gly His Val Gly Arg Gly Asn Ile His Val Ser Trp Pro Phe Val  
 20 25 30  
 Lys Val Ala Ile Ile Leu Ser Tyr Cys Gly Gln Gly Ala Trp Ile Leu  
 35 40 45  
 Ala Asn Lys Asn Ala Gly Asn Glu Leu Asn Pro Phe Phe Ala Ser Ile  
 50 55 60  
 Pro Ser Gln Phe Thr Met His Val Val Ile Leu Ala Thr Leu Ala Ala

65

70

75

80

Ile Ile Ala Ser Gln Ala Leu Ile Ser

85

&lt;210&gt; 12

&lt;211&gt; 378

&lt;212&gt; DNA

&lt;213&gt; group B streptococcus

&lt;220&gt;

&lt;221&gt; CDS

&lt;222&gt; (1)..(378)

&lt;400&gt; 12

atg cag gta ttt tta aat att gtc aat aaa ttc ttt gat cca gtt att 48  
 Met Gln Val Phe Leu Asn Ile Val Asn Lys Phe Phe Asp Pro Val Ile  
 1 5 10 15

cat atg ggt tgc gga gtt gtg atg cta att gtc atg aca ggt tta gcc 96  
 His Met Gly Ser Gly Val Val Met Leu Ile Val Met Thr Gly Leu Ala  
 20 25 30

atg ata ttt gga gtg aag ttt tct aaa gca ctt gaa ggt ggt att aag 144  
 Met Ile Phe Gly Val Lys Phe Ser Lys Ala Leu Glu Gly Gly Ile Lys  
 35 40 45

tta gct att gct ctt acg ggt att ggt gct att att ggt att tta act 192  
 Leu Ala Ile Ala Leu Thr Gly Ile Gly Ala Ile Ile Gly Ile Leu Thr  
 50 55 60

ggt gct ttt tcc gaa tca ctt caa gct ttt gtt aaa aat aca gga atc 240  
 Gly Ala Phe Ser Glu Ser Leu Gln Ala Phe Val Lys Asn Thr Gly Ile  
 65 70 75 80

aat cta agc att att gac gtt ggt tgg gct cca tta gca act att aca 288  
 Asn Leu Ser Ile Ile Asp Val Gly Trp Ala Pro Leu Ala Thr Ile Thr  
 85 90 95

tgg gga tca cca tat acg ctt tac ttc tta tta atc atg ctt att gtc 336  
 Trp Gly Ser Pro Tyr Thr Leu Tyr Phe Leu Leu Ile Met Leu Ile Val  
 100 105 110

aat att gtt atg att gtt atg aaa aaa aaa cgg ata cct tag 378  
 Asn Ile Val Met Ile Val Met Lys Lys Lys Arg Ile Pro  
 115 120 125

&lt;210&gt; 13

&lt;211&gt; 125

&lt;212&gt; PRT

&lt;213&gt; group B streptococcus

&lt;400&gt; 13

Met Gln Val Phe Leu Asn Ile Val Asn Lys Phe Phe Asp Pro Val Ile  
 1 5 10 15

His Met Gly Ser Gly Val Val Met Leu Ile Val Met Thr Gly Leu Ala  
 20 25 30

Met Ile Phe Gly Val Lys Phe Ser Lys Ala Leu Glu Gly Gly Ile Lys  
 35 40 45

Leu Ala Ile Ala Leu Thr Gly Ile Gly Ala Ile Ile Gly Ile Leu Thr  
 50 55 60

Gly Ala Phe Ser Glu Ser Leu Gln Ala Phe Val Lys Asn Thr Gly Ile  
 65 70 75 80

Asn Leu Ser Ile Ile Asp Val Gly Trp Ala Pro Leu Ala Thr Ile Thr  
 85 90 95

Trp Gly Ser Pro Tyr Thr Leu Tyr Phe Leu Leu Ile Met Leu Ile Val  
 100 105 110

Asn Ile Val Met Ile Val Met Lys Lys Lys Arg Ile Pro  
 115 120 125

&lt;210&gt; 14

&lt;211&gt; 705

&lt;212&gt; DNA

&lt;213&gt; group B streptococcus

&lt;220&gt;

&lt;221&gt; CDS

&lt;222&gt; (118)..(705)

&lt;400&gt; 14

ggatcgggcg caagcttaac gattcttttt aaaatcatta aatttttaaaa caaatttcag 60

acatattgcc aaagttttga tattattact ataatatagt ttgtagagga gaataat 117

atg ggc caa gaa cct atc atc gaa tat caa aat atc aat aaa gtg tat	165
Met Gly Gln Glu Pro Ile Ile Glu Tyr Gln Asn Ile Asn Lys Val Tyr	
1 5 10 15	
ggg gaa aat gtt gcg gtt gaa gat att aac ctt aaa att tac cct ggt	213
Gly Glu Asn Val Ala Val Glu Asp Ile Asn Leu Lys Ile Tyr Pro Gly	
20 25 30	
gat ttc gtt tgt ttc atc ggt acg agt gga tca ggt aaa aca aca tta	261
Asp Phe Val Cys Phe Ile Gly Thr Ser Gly Ser Gly Lys Thr Thr Leu	
35 40 45	
atg cgt atg gtt aac cat atg tta aaa cca aca aat ggt act cta tta	309
Met Arg Met Val Asn His Met Leu Lys Pro Thr Asn Gly Thr Leu Leu	
50 55 60	
ttt aag gga aaa gat atc tct act att aac ccc att gaa tta aga cgc	357
Phe Lys Gly Lys Asp Ile Ser Thr Ile Asn Pro Ile Glu Leu Arg Arg	
65 70 75 80	
aga att gga tat gtt atc caa aac att ggt tta atg cct cat atg acc	405
Arg Ile Gly Tyr Val Ile Gln Asn Ile Gly Leu Met Pro His Met Thr	
85 90 95	
att tac gaa aat ata gtt ctt gta cca aaa tta ttg aaa tgg tca gaa	453
Ile Tyr Glu Asn Ile Val Leu Val Pro Lys Leu Leu Lys Trp Ser Glu	
100 105 110	
gaa gct aaa aga gct aaa gca agg gaa ctt att aaa tta gtt gaa tta	501
Glu Ala Lys Arg Ala Lys Ala Arg Glu Leu Ile Lys Leu Val Glu Leu	
115 120 125	
ccc gaa gaa tat ttg gat cgc tac cct agt gag ttg tct ggc ggt cag	549
Pro Glu Glu Tyr Leu Asp Arg Tyr Pro Ser Glu Leu Ser Gly Gly Gln	
130 135 140	
caa caa cgt atc ggt gtc att cgc gct ctt gca gca gac caa gat att	597
Gln Gln Arg Ile Gly Val Ile Arg Ala Leu Ala Ala Asp Gln Asp Ile	
145 150 155 160	
att tta atg gat gag cct ttt gga gct ctg gat cct att act aga gaa	645
Ile Leu Met Asp Glu Pro Phe Gly Ala Leu Asp Pro Ile Thr Arg Glu	
165 170 175	
ggt att caa gac ttt agt caa gtc tct tca gga aga aat ggg gga aaa	693
Gly Ile Gln Asp Phe Ser Gln Val Ser Ser Gly Arg Asn Gly Gly Lys	
180 185 190	

cta tca tct tag  
 Leu Ser Ser  
 195

705

<210> 15  
 <211> 195  
 <212> PRT  
 <213> group B streptococcus

<400> 15  
 Met Gly Gln Glu Pro Ile Ile Glu Tyr Gln Asn Ile Asn Lys Val Tyr  
 1 5 10 15

Gly Glu Asn Val Ala Val Glu Asp Ile Asn Leu Lys Ile Tyr Pro Gly  
 20 25 30

Asp Phe Val Cys Phe Ile Gly Thr Ser Gly Ser Gly Lys Thr Thr Leu  
 35 40 45

Met Arg Met Val Asn His Met Leu Lys Pro Thr Asn Gly Thr Leu Leu  
 50 55 60

Phe Lys Gly Lys Asp Ile Ser Thr Ile Asn Pro Ile Glu Leu Arg Arg  
 65 70 75 80

Arg Ile Gly Tyr Val Ile Gln Asn Ile Gly Leu Met Pro His Met Thr  
 85 90 95

Ile Tyr Glu Asn Ile Val Leu Val Pro Lys Leu Leu Lys Trp Ser Glu  
 100 105 110

Glu Ala Lys Arg Ala Lys Ala Arg Glu Leu Ile Lys Leu Val Glu Leu  
 115 120 125

Pro Glu Glu Tyr Leu Asp Arg Tyr Pro Ser Glu Leu Ser Gly Gly Gln  
 130 135 140

Gln Gln Arg Ile Gly Val Ile Arg Ala Leu Ala Ala Asp Gln Asp Ile  
 145 150 155 160

Ile Leu Met Asp Glu Pro Phe Gly Ala Leu Asp Pro Ile Thr Arg Glu  
 165 170 175

Gly Ile Gln Asp Phe Ser Gln Val Ser Ser Gly Arg Asn Gly Gly Lys  
 180 185 190

Leu Ser Ser

195

&lt;210&gt; 16

&lt;211&gt; 367

&lt;212&gt; DNA

&lt;213&gt; group B streptococcus

&lt;220&gt;

&lt;221&gt; CDS

&lt;222&gt; (1)..(366)

&lt;400&gt; 16

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atc cct tat agt gat gtt ttt gct aca gga gga ttt tta tac tat gta 48
Ile Pro Tyr Ser Asp Val Phe Ala Thr Gly Gly Phe Leu Tyr Tyr Val
  1           5           10          15

acg att gct cta agt tac ctt tta ggg tct agt atc tgg tta ttt att 96
Thr Ile Ala Leu Ser Tyr Leu Leu Gly Ser Ser Ile Trp Leu Phe Ile
      20           25           30

gta cag ttt att gct tac tat gta tct gga att tat ttt tat aaa tta 144
Val Gln Phe Ile Ala Tyr Tyr Val Ser Gly Ile Tyr Phe Tyr Lys Leu
      35           40           45

gtt tat tat gtg gca caa agt gaa att gtc tcg ata ggc atg acg ttg 192
Val Tyr Tyr Val Ala Gln Ser Glu Ile Val Ser Ile Gly Met Thr Leu
      50           55           60

att ttc tat ata atg aat att gtc tta gga ttc ggt ggt atg tac cca 240
Ile Phe Tyr Ile Met Asn Ile Val Leu Gly Phe Gly Gly Met Tyr Pro
      65           70           75           80

ata cag tgg gca tta cct ttt atg ctc att tcg cta tgg ttt tta att 288
Ile Gln Trp Ala Leu Pro Phe Met Leu Ile Ser Leu Trp Phe Leu Ile
      85           90           95

aaa ttt tgt gtc gat aat atc gtt gat gaa gca ttt ata ttt tat ggt 336
Lys Phe Cys Val Asp Asn Ile Val Asp Glu Ala Phe Ile Phe Tyr Gly
      100          105          110

att tta gca gca ttc tca cta ttt ata gat c 367
Ile Leu Ala Ala Phe Ser Leu Phe Ile Asp
      115          120

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&lt;210&gt; 17

&lt;211&gt; 122

&lt;212&gt; PRT

&lt;213&gt; group B streptococcus

&lt;400&gt; 17

Ile Pro Tyr Ser Asp Val Phe Ala Thr Gly Gly Phe Leu Tyr Tyr Val  
 1 5 10 15

Thr Ile Ala Leu Ser Tyr Leu Leu Gly Ser Ser Ile Trp Leu Phe Ile  
 20 25 30

Val Gln Phe Ile Ala Tyr Tyr Val Ser Gly Ile Tyr Phe Tyr Lys Leu  
 35 40 45

Val Tyr Tyr Val Ala Gln Ser Glu Ile Val Ser Ile Gly Met Thr Leu  
 50 55 60

Ile Phe Tyr Ile Met Asn Ile Val Leu Gly Phe Gly Gly Met Tyr Pro  
 65 70 75 80

Ile Gln Trp Ala Leu Pro Phe Met Leu Ile Ser Leu Trp Phe Leu Ile  
 85 90 95

Lys Phe Cys Val Asp Asn Ile Val Asp Glu Ala Phe Ile Phe Tyr Gly  
 100 105 110

Ile Leu Ala Ala Phe Ser Leu Phe Ile Asp  
 115 120

&lt;210&gt; 18

&lt;211&gt; 570

&lt;212&gt; DNA

&lt;213&gt; group B streptococcus

&lt;220&gt;

&lt;221&gt; CDS

&lt;222&gt; (1)..(570)

&lt;400&gt; 18

atg agg aaa cgt ttt tcc ttg cta aat ttt att gtt gtt act ttt att 48  
 Met Arg Lys Arg Phe Ser Leu Leu Asn Phe Ile Val Val Thr Phe Ile  
 1 5 10 15

ttc ttt ttc ttt att ctt ttt ccg ctt tta aac cat aag gga aaa gta 96  
 Phe Phe Phe Phe Ile Leu Phe Pro Leu Leu Asn His Lys Gly Lys Val  
 20 25 30



gat gct aat tct agg cag agt gtt acc tac acc aaa gaa gaa ttt ata 144  
Asp Ala Asn Ser Arg Gln Ser Val Thr Tyr Thr Lys Glu Glu Phe Ile  
35 40 45

caa aaa att gtg cca gat gcg caa gat cta gga aag tcg tac ggt att 192  
Gln Lys Ile Val Pro Asp Ala Gln Asp Leu Gly Lys Ser Tyr Gly Ile  
50 55 60

cgt cct tca ttt att att gca cag gcg gct ttg gat tct gat ttc gga 240  
Arg Pro Ser Phe Ile Ile Ala Gln Ala Ala Leu Asp Ser Asp Phe Gly  
65 70 75 80

gag aaa tat agc tat agt atc ata atc tgt tgg ttg ctt gca gaa cca 288  
Glu Lys Tyr Ser Tyr Ser Ile Ile Ile Cys Trp Leu Leu Ala Glu Pro  
85 90 95

gga acg ccc tca att acc tta aat gat agt agt aca gga aaa aaa cag 336  
Gly Thr Pro Ser Ile Thr Leu Asn Asp Ser Ser Thr Gly Lys Lys Gln  
100 105 110

gaa aag caa ttt act cat tat aaa tct tgg aag tat tca atg gat gat 384  
Glu Lys Gln Phe Thr His Tyr Lys Ser Trp Lys Tyr Ser Met Asp Asp  
115 120 125

tac ctt gct cat ata aaa tct gga gcg aca ggc aaa aaa gat tca tat 432  
Tyr Leu Ala His Ile Lys Ser Gly Ala Thr Gly Lys Lys Asp Ser Tyr  
130 135 140

act ata atg gtg tct gtt aaa aat cca aaa act tta gtg caa aaa tta 480  
Thr Ile Met Val Ser Val Lys Asn Pro Lys Thr Leu Val Gln Lys Leu  
145 150 155 160

caa gat agt ggt ttt gat aat gac aaa aag tac gct aaa aaa atg acg 528  
Gln Asp Ser Gly Phe Asp Asn Asp Lys Lys Tyr Ala Lys Lys Met Thr  
165 170 175

gaa atc att gat ttg tat gat tta aca aga tat gat aag tga 570  
Glu Ile Ile Asp Leu Tyr Asp Leu Thr Arg Tyr Asp Lys  
180 185 190

&lt;210&gt; 19

&lt;211&gt; 189

&lt;212&gt; PRT

&lt;213&gt; group B streptococcus

&lt;400&gt; 19

Met Arg Lys Arg Phe Ser Leu Leu Asn Phe Ile Val Val Thr Phe Ile  
 1 5 10 15  
 Phe Phe Phe Phe Ile Leu Phe Pro Leu Leu Asn His Lys Gly Lys Val  
 20 25 30  
 Asp Ala Asn Ser Arg Gln Ser Val Thr Tyr Thr Lys Glu Glu Phe Ile  
 35 40 45  
 Gln Lys Ile Val Pro Asp Ala Gln Asp Leu Gly Lys Ser Tyr Gly Ile  
 50 55 60  
 Arg Pro Ser Phe Ile Ile Ala Gln Ala Ala Leu Asp Ser Asp Phe Gly  
 65 70 75 80  
 Glu Lys Tyr Ser Tyr Ser Ile Ile Ile Cys Trp Leu Leu Ala Glu Pro  
 85 90 95  
 Gly Thr Pro Ser Ile Thr Leu Asn Asp Ser Ser Thr Gly Lys Lys Gln  
 100 105 110  
 Glu Lys Gln Phe Thr His Tyr Lys Ser Trp Lys Tyr Ser Met Asp Asp  
 115 120 125  
 Tyr Leu Ala His Ile Lys Ser Gly Ala Thr Gly Lys Lys Asp Ser Tyr  
 130 135 140  
 Thr Ile Met Val Ser Val Lys Asn Pro Lys Thr Leu Val Gln Lys Leu  
 145 150 155 160  
 Gln Asp Ser Gly Phe Asp Asn Asp Lys Lys Tyr Ala Lys Lys Met Thr  
 165 170 175  
 Glu Ile Ile Asp Leu Tyr Asp Leu Thr Arg Tyr Asp Lys  
 180 185

&lt;210&gt; 20

&lt;211&gt; 978

&lt;212&gt; DNA

&lt;213&gt; group B streptococcus

&lt;220&gt;

&lt;221&gt; CDS

&lt;222&gt; (1)..(978)

&lt;400&gt; 20

atg ctt gtc atc att ttg atc att gta cta gct agt ctg aca gtg acg	48
Met Leu Val Ile Ile Leu Ile Ile Val Leu Ala Ser Leu Thr Val Thr	
1 5 10 15	
ata att tct tac cca aaa atg acg gaa tta aca aag tcc gtt gaa aaa	96
Ile Ile Ser Tyr Pro Lys Met Thr Glu Leu Thr Lys Ser Val Glu Lys	
20 25 30	
caa ctt gaa gat aat gct gat aat cta tca gac caa ctg aca tat cag	144
Gln Leu Glu Asp Asn Ala Asp Asn Leu Ser Asp Gln Leu Thr Tyr Gln	
35 40 45	
ata gaa gtg gcg caa aaa gat caa atc tac gtg act aat cag cta aac	192
Ile Glu Val Ala Gln Lys Asp Gln Ile Tyr Val Thr Asn Gln Leu Asn	
50 55 60	
cgt atg caa cag gaa att atc agt cgc tta ccg ata tgc gta cag aat	240
Arg Met Gln Gln Glu Ile Ile Ser Arg Leu Pro Ile Cys Val Gln Asn	
65 70 75 80	
aaa tca gca tta acg gag agt cga gat cga tca gac aaa cgc ttg gaa	288
Lys Ser Ala Leu Thr Glu Ser Arg Asp Arg Ser Asp Lys Arg Leu Glu	
85 90 95	
ttg att aac tcc aat tta tct cag tca gtt cag aaa atg caa gat tca	336
Leu Ile Asn Ser Asn Leu Ser Gln Ser Val Gln Lys Met Gln Asp Ser	
100 105 110	
atg aaa aac gct tgg atc aaa tgc gcc aaa ctg ttg agg aaa agc tgg	384
Met Lys Asn Ala Trp Ile Lys Cys Ala Lys Leu Leu Arg Lys Ser Trp	
115 120 125	
aaa aaa cgc tac aaa cgc gtt gca aac ttc ttt gaa act gta tcg cgt	432
Lys Lys Arg Tyr Lys Arg Val Ala Asn Phe Phe Glu Thr Val Ser Arg	
130 135 140	
caa cta gag agc gtc aat caa ggt ctg ggt aga tgg aaa ctg tgc caa	480
Gln Leu Glu Ser Val Asn Gln Gly Leu Gly Arg Trp Lys Leu Cys Gln	
145 150 155 160	
gat gtt ggt acc act gaa caa agt ctg tca aat act aag aca agg gga	528
Asp Val Gly Thr Thr Glu Gln Ser Leu Ser Asn Thr Lys Thr Arg Gly	
165 170 175	
ata tta ggg gag tta caa ctc ggt caa att ata gaa gat att atg aca	576
Ile Leu Gly Glu Leu Gln Leu Gly Gln Ile Ile Glu Asp Ile Met Thr	
180 185 190	

gtt agt caa tat gag aga gaa ttt cct acg gtg tct ggc tct tct gag 624  
 Val Ser Gln Tyr Glu Arg Glu Phe Pro Thr Val Ser Gly Ser Ser Glu  
 195 200 205

cgt gtt gaa tat gct att aaa tac ctg gaa atg gtc agg gag att ata 672  
 Arg Val Glu Tyr Ala Ile Lys Tyr Leu Glu Met Val Arg Glu Ile Ile  
 210 215 220

tct att tgc cta ttg act cta agt ttc tct aga aga tta tta ccg att 720  
 Ser Ile Cys Leu Leu Thr Leu Ser Phe Ser Arg Arg Leu Leu Pro Ile  
 225 230 235 240

ggg aga tgc tta tgg aat tgg gtg acc agg ttc aaa tgg aac tct att 768  
 Gly Arg Cys Leu Trp Asn Trp Val Thr Arg Phe Lys Trp Asn Ser Ile  
 245 250 255

cgt aat ctt tac tgg gca agt att cgt aaa ttt gca aaa gat ata aac 816  
 Arg Asn Leu Tyr Trp Ala Ser Ile Arg Lys Phe Ala Lys Asp Ile Asn  
 260 265 270

aat aag tac tta aat cct cct gaa acg aca aat ttt ggt atc atg ttc 864  
 Asn Lys Tyr Leu Asn Pro Pro Glu Thr Thr Asn Phe Gly Ile Met Phe  
 275 280 285

tta cca act gaa ggg ctc tat tct gaa gtg gta aga aat gca aca ttc 912  
 Leu Pro Thr Glu Gly Leu Tyr Ser Glu Val Val Arg Asn Ala Thr Phe  
 290 295 300

ttt gat agt cta aga cgt gac gaa aat att gta gta gct gga ccg tca 960  
 Phe Asp Ser Leu Arg Arg Asp Glu Asn Ile Val Val Ala Gly Pro Ser  
 305 310 315 320

acc tta tct gct tac taa 978  
 Thr Leu Ser Ala Tyr  
 325

&lt;210&gt; 21

&lt;211&gt; 325

&lt;212&gt; PRT

&lt;213&gt; group B streptococcus

&lt;400&gt; 21

Met Leu Val Ile Ile Leu Ile Ile Val Leu Ala Ser Leu Thr Val Thr  
 1 5 10 15

Ile Ile Ser Tyr Pro Lys Met Thr Glu Leu Thr Lys Ser Val Glu Lys  
 20 25 30

Gln Leu Glu Asp Asn Ala Asp Asn Leu Ser Asp Gln Leu Thr Tyr Gln  
 35 40 45  
 Ile Glu Val Ala Gln Lys Asp Gln Ile Tyr Val Thr Asn Gln Leu Asn  
 50 55 60  
 Arg Met Gln Gln Glu Ile Ile Ser Arg Leu Pro Ile Cys Val Gln Asn  
 65 70 75 80  
 Lys Ser Ala Leu Thr Glu Ser Arg Asp Arg Ser Asp Lys Arg Leu Glu  
 85 90 95  
 Leu Ile Asn Ser Asn Leu Ser Gln Ser Val Gln Lys Met Gln Asp Ser  
 100 105 110  
 Met Lys Asn Ala Trp Ile Lys Cys Ala Lys Leu Leu Arg Lys Ser Trp  
 115 120 125  
 Lys Lys Arg Tyr Lys Arg Val Ala Asn Phe Phe Glu Thr Val Ser Arg  
 130 135 140  
 Gln Leu Glu Ser Val Asn Gln Gly Leu Gly Arg Trp Lys Leu Cys Gln  
 145 150 155 160  
 Asp Val Gly Thr Thr Glu Gln Ser Leu Ser Asn Thr Lys Thr Arg Gly  
 165 170 175  
 Ile Leu Gly Glu Leu Gln Leu Gly Gln Ile Ile Glu Asp Ile Met Thr  
 180 185 190  
 Val Ser Gln Tyr Glu Arg Glu Phe Pro Thr Val Ser Gly Ser Ser Glu  
 195 200 205  
 Arg Val Glu Tyr Ala Ile Lys Tyr Leu Glu Met Val Arg Glu Ile Ile  
 210 215 220  
 Ser Ile Cys Leu Leu Thr Leu Ser Phe Ser Arg Arg Leu Leu Pro Ile  
 225 230 235 240  
 Gly Arg Cys Leu Trp Asn Trp Val Thr Arg Phe Lys Trp Asn Ser Ile  
 245 250 255  
 Arg Asn Leu Tyr Trp Ala Ser Ile Arg Lys Phe Ala Lys Asp Ile Asn  
 260 265 270  
 Asn Lys Tyr Leu Asn Pro Pro Glu Thr Thr Asn Phe Gly Ile Met Phe  
 275 280 285

Leu Pro Thr Glu Gly Leu Tyr Ser Glu Val Val Arg Asn Ala Thr Phe  
 290 295 300

Phe Asp Ser Leu Arg Arg Asp Glu Asn Ile Val Val Ala Gly Pro Ser  
 305 310 315 320

Thr Leu Ser Ala Tyr  
 325

<210> 22

<211> 579

<212> DNA

<213> group B streptococcus

<220>

<221> CDS

<222> (1)..(579)

<400> 22

atg cga aaa gaa gtg aca cca gag atg ctt aac tat aat aag tat cct 48  
 Met Arg Lys Glu Val Thr Pro Glu Met Leu Asn Tyr Asn Lys Tyr Pro  
 1 5 10 15

ggc cca cag ttt att cac ttt gaa aat atc gtt aaa agt gat gat att 96  
 Gly Pro Gln Phe Ile His Phe Glu Asn Ile Val Lys Ser Asp Asp Ile  
 20 25 30

gaa ttt caa ctt gtt att aat gaa aaa tca gct ttt gat gtg act gtc 144  
 Glu Phe Gln Leu Val Ile Asn Glu Lys Ser Ala Phe Asp Val Thr Val  
 35 40 45

ttt gga caa cgt ttt tct gag att tta tta aaa tat gat ttt atc gtt 192  
 Phe Gly Gln Arg Phe Ser Glu Ile Leu Leu Lys Tyr Asp Phe Ile Val  
 50 55 60

ggc gat tgg ggt aac gag cag ttg agg cta aga ggc ttt tac aaa gat 240  
 Gly Asp Trp Gly Asn Glu Gln Leu Arg Leu Arg Gly Phe Tyr Lys Asp  
 65 70 75 80

gct agt acg att aga aaa aat agc cgg att tca cgt tta gaa gat tat 288  
 Ala Ser Thr Ile Arg Lys Asn Ser Arg Ile Ser Arg Leu Glu Asp Tyr  
 85 90 95

att aaa gag tat tgt aac ttt ggt tgt gct tat ttt gtg ttg gag aat 336  
 Ile Lys Glu Tyr Cys Asn Phe Gly Cys Ala Tyr Phe Val Leu Glu Asn

100	105	110	
cca aat cct aga gat att aaa ttt gat gat gaa aga cct cat aag cgt			384
Pro Asn Pro Arg Asp Ile Lys Phe Asp Asp Glu Arg Pro His Lys Arg			
115	120	125	
cgt aag tca aga tcc aaa tca caa tca tca aag tca caa act aga aat			432
Arg Lys Ser Arg Ser Lys Ser Gln Ser Ser Lys Ser Gln Thr Arg Asn			
130	135	140	
aat cgt tcc cag tca aat gcc aat gct cat ttt aca agt aaa aag cgt			480
Asn Arg Ser Gln Ser Asn Ala Asn Ala His Phe Thr Ser Lys Lys Arg			
145	150	155	160
aaa gac aca aaa cgc cgt caa gaa cgt cat att aaa gaa gag caa gat			528
Lys Asp Thr Lys Arg Arg Gln Glu Arg His Ile Lys Glu Glu Gln Asp			
165	170	175	
aag gaa atg acc tct gca aag cag cat ttg tta ttc gta aga aaa aat			576
Lys Glu Met Thr Ser Ala Lys Gln His Leu Leu Phe Val Arg Lys Asn			
180	185	190	
taa			579

&lt;210&gt; 23

&lt;211&gt; 192

&lt;212&gt; PRT

&lt;213&gt; group B streptococcus

&lt;400&gt; 23

Met Arg Lys Glu Val Thr Pro Glu Met Leu Asn Tyr Asn Lys Tyr Pro

1

5

10

15

Gly Pro Gln Phe Ile His Phe Glu Asn Ile Val Lys Ser Asp Asp Ile

20

25

30

Glu Phe Gln Leu Val Ile Asn Glu Lys Ser Ala Phe Asp Val Thr Val

35

40

45

Phe Gly Gln Arg Phe Ser Glu Ile Leu Leu Lys Tyr Asp Phe Ile Val

50

55

60

Gly Asp Trp Gly Asn Glu Gln Leu Arg Leu Arg Gly Phe Tyr Lys Asp

65

70

75

80

Ala Ser Thr Ile Arg Lys Asn Ser Arg Ile Ser Arg Leu Glu Asp Tyr

	85		90		95
Ile Lys Glu Tyr Cys Asn Phe Gly Cys Ala Tyr Phe Val Leu Glu Asn					
	100		105		110
Pro Asn Pro Arg Asp Ile Lys Phe Asp Asp Glu Arg Pro His Lys Arg					
	115		120		125
Arg Lys Ser Arg Ser Lys Ser Gln Ser Ser Lys Ser Gln Thr Arg Asn					
	130		135		140
Asn Arg Ser Gln Ser Asn Ala Asn Ala His Phe Thr Ser Lys Lys Arg					
	145		150		155
					160
Lys Asp Thr Lys Arg Arg Gln Glu Arg His Ile Lys Glu Glu Gln Asp					
		165		170	175
Lys Glu Met Thr Ser Ala Lys Gln His Leu Leu Phe Val Arg Lys Asn					
	180		185		190

&lt;210&gt; 24

&lt;211&gt; 609

&lt;212&gt; DNA

&lt;213&gt; group B streptococcus

&lt;220&gt;

&lt;221&gt; CDS

&lt;222&gt; (1)..(609)

&lt;400&gt; 24

atg aca ata aaa aaa gtg tta agt gta aca gga att att tta gtg aca	48
Met Thr Ile Lys Lys Val Leu Ser Val Thr Gly Ile Ile Leu Val Thr	
1 5 10 15	

gta gcg tct cta gct gct tgt agc tca aaa tct cat act act aag acg	96
Val Ala Ser Leu Ala Ala Cys Ser Ser Lys Ser His Thr Thr Lys Thr	
20 25 30	

ggc aaa aaa gaa gtt aat ttt gca act gtt gga aca acg gca cct ttt	144
Gly Lys Lys Glu Val Asn Phe Ala Thr Val Gly Thr Thr Ala Pro Phe	
35 40 45	

tct tat gtg aag gat ggg aaa ctg act ggc ttt gat att gaa gta gcc	192
Ser Tyr Val Lys Asp Gly Lys Leu Thr Gly Phe Asp Ile Glu Val Ala	
50 55 60	



aaa gct gtt ttt aaa ggt tca gat aac tat aaa gtc act ttt aaa aaa 240  
 Lys Ala Val Phe Lys Gly Ser Asp Asn Tyr Lys Val Thr Phe Lys Lys  
 65 70 75 80

aca gaa tgg tca tcg gta ttt acc ggc att gat tca gga aag ttt caa 288  
 Thr Glu Trp Ser Ser Val Phe Thr Gly Ile Asp Ser Gly Lys Phe Gln  
 85 90 95

atg ggt gga aat aat att tct tat tca tca gag aga tct caa aaa tay 336  
 Met Gly Gly Asn Asn Ile Ser Tyr Ser Ser Glu Arg Ser Gln Lys Tyr  
 100 105 110

tta ttt tca tac cca ata ggc tct act cct tca gtt tta gca gtt cct 384  
 Leu Phe Ser Tyr Pro Ile Gly Ser Thr Pro Ser Val Leu Ala Val Pro  
 115 120 125

aag aat agt aat atc aaa gct tat aat gat att agt ggt cat aaa aca 432  
 Lys Asn Ser Asn Ile Lys Ala Tyr Asn Asp Ile Ser Gly His Lys Thr  
 130 135 140

cag gtt gtc caa gga acg aca act gcc aag caa tta gaa aat ttc aat 480  
 Gln Val Val Gln Gly Thr Thr Thr Ala Lys Gln Leu Glu Asn Phe Asn  
 145 150 155 160

aaa gag cat cag aaa aat cct gtt act cta aaa tat act aat gaa aat 528  
 Lys Glu His Gln Lys Asn Pro Val Thr Leu Lys Tyr Thr Asn Glu Asn  
 165 170 175

att aca cag att cta acg aat ttg agt gat gga aaa gct gat ttt aaa 576  
 Ile Thr Gln Ile Leu Thr Asn Leu Ser Asp Gly Lys Ala Asp Phe Lys  
 180 185 190

ctt ttg acg gac caa ctg tta acg cta tta taa 609  
 Leu Leu Thr Asp Gln Leu Leu Thr Leu Leu  
 195 200

<210> 25

<211> 202

<212> PRT

<213> group B streptococcus

<400> 25

Met Thr Ile Lys Lys Val Leu Ser Val Thr Gly Ile Ile Leu Val Thr  
 1 5 10 15

Val Ala Ser Leu Ala Ala Cys Ser Ser Lys Ser His Thr Thr Lys Thr  
 20 25 30

Gly Lys Lys Glu Val Asn Phe Ala Thr Val Gly Thr Thr Ala Pro Phe  
 35 40 45

Ser Tyr Val Lys Asp Gly Lys Leu Thr Gly Phe Asp Ile Glu Val Ala  
 50 55 60

Lys Ala Val Phe Lys Gly Ser Asp Asn Tyr Lys Val Thr Phe Lys Lys  
 65 70 75 80

Thr Glu Trp Ser Ser Val Phe Thr Gly Ile Asp Ser Gly Lys Phe Gln  
 85 90 95

Met Gly Gly Asn Asn Ile Ser Tyr Ser Ser Glu Arg Ser Gln Lys Tyr  
 100 105 110

Leu Phe Ser Tyr Pro Ile Gly Ser Thr Pro Ser Val Leu Ala Val Pro  
 115 120 125

Lys Asn Ser Asn Ile Lys Ala Tyr Asn Asp Ile Ser Gly His Lys Thr  
 130 135 140

Gln Val Val Gln Gly Thr Thr Thr Ala Lys Gln Leu Glu Asn Phe Asn  
 145 150 155 160

Lys Glu His Gln Lys Asn Pro Val Thr Leu Lys Tyr Thr Asn Glu Asn  
 165 170 175

Ile Thr Gln Ile Leu Thr Asn Leu Ser Asp Gly Lys Ala Asp Phe Lys  
 180 185 190

Leu Leu Thr Asp Gln Leu Leu Thr Leu Leu  
 195 200

<210> 26

<211> 357

<212> DNA

<213> group B streptococcus

<220>

<221> CDS

<222> (1)..(357)

<400> 26

atg aag aat ata aca aag cta tca act gtt gct tta agc cta cta ctt 48  
 Met Lys Asn Ile Thr Lys Leu Ser Thr Val Ala Leu Ser Leu Leu Leu

1	5	10	15	
tgt acg gcg tgt gct gca tca aac acg tct aca tct aaa aca cag tct	96			
Cys Thr Ala Cys Ala Ala Ser Asn Thr Ser Thr Ser Lys Thr Gln Ser				
20	25	30		
cat cat cct aaa caa act aaa ctc aca gat aag caa aaa gaa gaa ccc	144			
His His Pro Lys Gln Thr Lys Leu Thr Asp Lys Gln Lys Glu Glu Pro				
35	40	45		
aaa aac aaa gaa gct gct gat caa gag atg cat ccc caa ggc gct gtt	192			
Lys Asn Lys Glu Ala Ala Asp Gln Glu Met His Pro Gln Gly Ala Val				
50	55	60		
gat ttg aca aaa tat aag gca aaa ccg gtc aaa gat tat gga aaa aaa	240			
Asp Leu Thr Lys Tyr Lys Ala Lys Pro Val Lys Asp Tyr Gly Lys Lys				
65	70	75	80	
atc gat gtt ggt gat ggc aag aaa atg aac att tat gaa act ggt cag	288			
Ile Asp Val Gly Asp Gly Lys Lys Met Asn Ile Tyr Glu Thr Gly Gln				
85	90	95		
gga aaa att cca att gtt ttt att cct ggt caa gct gag att cgc cac	336			
Gly Lys Ile Pro Ile Val Phe Ile Pro Gly Gln Ala Glu Ile Arg His				
100	105	110		
gct atg ctt ata aga att taa	357			
Ala Met Leu Ile Arg Ile				
115				

&lt;210&gt; 27

&lt;211&gt; 118

&lt;212&gt; PRT

&lt;213&gt; group B streptococcus

&lt;400&gt; 27

Met Lys Asn Ile Thr Lys Leu Ser Thr Val Ala Leu Ser Leu Leu Leu				
1	5	10	15	
Cys Thr Ala Cys Ala Ala Ser Asn Thr Ser Thr Ser Lys Thr Gln Ser				
20	25	30		
His His Pro Lys Gln Thr Lys Leu Thr Asp Lys Gln Lys Glu Glu Pro				
35	40	45		
Lys Asn Lys Glu Ala Ala Asp Gln Glu Met His Pro Gln Gly Ala Val				
50	55	60		

Asp Leu Thr Lys Tyr Lys Ala Lys Pro Val Lys Asp Tyr Gly Lys Lys  
 65 70 75 80

Ile Asp Val Gly Asp Gly Lys Lys Met Asn Ile Tyr Glu Thr Gly Gln  
 85 90 95

Gly Lys Ile Pro Ile Val Phe Ile Pro Gly Gln Ala Glu Ile Arg His  
 100 105 110

Ala Met Leu Ile Arg Ile  
 115

<210> 28

<211> 1191

<212> DNA

<213> group B streptococcus

<220>

<221> CDS

<222> (1)..(1191)

<400> 28

gtg aat gaa tcg acc atc aga aaa gaa ttt aaa ata gtt gtt ttt aaa 48  
 Val Asn Glu Ser Thr Ile Arg Lys Glu Phe Lys Ile Val Val Phe Lys  
 1 5 10 15

tgg atc tta aat aat caa gca gtt att gct ctc atg att acc ttt ttg 96  
 Trp Ile Leu Asn Asn Gln Ala Val Ile Ala Leu Met Ile Thr Phe Leu  
 20 25 30

gta ttt tta acg att ttt att ttt acc aaa atc tct ttt atg ttt aaa 144  
 Val Phe Leu Thr Ile Phe Ile Phe Thr Lys Ile Ser Phe Met Phe Lys  
 35 40 45

cct gtg ttt gat ttt ctt gct gtg ctg ata ttg ccg ctt gta att tct 192  
 Pro Val Phe Asp Phe Leu Ala Val Leu Ile Leu Pro Leu Val Ile Ser  
 50 55 60

ggc ttg ctt tat tac cta tta aaa cct atg gtt aca ttt tta gag aag 240  
 Gly Leu Leu Tyr Tyr Leu Leu Lys Pro Met Val Thr Phe Leu Glu Lys  
 65 70 75 80

cgg gga att aag cgt gta aca gcg ata tta tca gtt ttt act att ata 288  
 Arg Gly Ile Lys Arg Val Thr Ala Ile Leu Ser Val Phe Thr Ile Ile  
 85 90 95

atc ctt ctg tta att tgg gca atg tct agt ttt att ccc atg atg agt 336  
 Ile Leu Leu Leu Ile Trp Ala Met Ser Ser Phe Ile Pro Met Met Ser  
 100 105 110

aat caa tta cgc cat ttt atg gaa gat ctc cct tca tat gtg aat aaa 384  
 Asn Gln Leu Arg His Phe Met Glu Asp Leu Pro Ser Tyr Val Asn Lys  
 115 120 125

gtg caa atg gaa aca agt tcg ttt ata gat cac aac cct tgg tta aaa 432  
 Val Gln Met Glu Thr Ser Ser Phe Ile Asp His Asn Pro Trp Leu Lys  
 130 135 140

tct tat aaa ggg gaa ata tcg agc atg tta tct aat atc agt agc caa 480  
 Ser Tyr Lys Gly Glu Ile Ser Ser Met Leu Ser Asn Ile Ser Ser Gln  
 145 150 155 160

gcg gtc tct tat gct gaa aaa ttt tca aag aat gtt tta gat tgg gca 528  
 Ala Val Ser Tyr Ala Glu Lys Phe Ser Lys Asn Val Leu Asp Trp Ala  
 165 170 175

gga aat tta gct agt aca gtt gca cgt gtg aca gta gca aca atc atg 576  
 Gly Asn Leu Ala Ser Thr Val Ala Arg Val Thr Val Ala Thr Ile Met  
 180 185 190

gct ccc ttt att ttg ttt tat ctt tta aga gat agt cgc aac atg aag 624  
 Ala Pro Phe Ile Leu Phe Tyr Leu Leu Arg Asp Ser Arg Asn Met Lys  
 195 200 205

aat ggt ttc tta atg gtt tta cca acc aaa cta cgc caa cca gct gat 672  
 Asn Gly Phe Leu Met Val Leu Pro Thr Lys Leu Arg Gln Pro Ala Asp  
 210 215 220

cgt att ttg cga gaa atg aat agt caa atg tca gga tat gtg caa gga 720  
 Arg Ile Leu Arg Glu Met Asn Ser Gln Met Ser Gly Tyr Val Gln Gly  
 225 230 235 240

caa atc att gtt gct att act gtt ggt gtt att ttt tca ata atg tat 768  
 Gln Ile Ile Val Ala Ile Thr Val Gly Val Ile Phe Ser Ile Met Tyr  
 245 250 255

agt att ata ggc ctt aga tat ggc gtg aca tta ggg att att gcc ggt 816  
 Ser Ile Ile Gly Leu Arg Tyr Gly Val Thr Leu Gly Ile Ile Ala Gly  
 260 265 270

gtg tta aat atg gtt ccc tat ttg gga agt ttt gtc gcc caa att cca 864  
 Val Leu Asn Met Val Pro Tyr Leu Gly Ser Phe Val Ala Gln Ile Pro  
 275 280 285

gtg ttt atc tta gcg ctt gtc gca gga cct gtt atg gtt gtt aaa gtt 912  
Val Phe Ile Leu Ala Leu Val Ala Gly Pro Val Met Val Val Lys Val  
290 295 300

gcg att gtt ttt gtt att gag caa act cta gag gga cgc ttt gtc tca 960  
Ala Ile Val Phe Val Ile Glu Gln Thr Leu Glu Gly Arg Phe Val Ser  
305 310 315 320

cct ttg gtt tta ggt aat aaa ctt agc att cat cca att aca att atg 1008  
Pro Leu Val Leu Gly Asn Lys Leu Ser Ile His Pro Ile Thr Ile Met  
325 330 335

ttt att tta tta acc tct gga gcg atg ttt ggt gtt tgg gga gta ttc 1056  
Phe Ile Leu Leu Thr Ser Gly Ala Met Phe Gly Val Trp Gly Val Phe  
340 345 350

ctc agt att ccg att tat gca tct atc aaa gtt gtt gtt aaa gaa ttg 1104  
Leu Ser Ile Pro Ile Tyr Ala Ser Ile Lys Val Val Val Lys Glu Leu  
355 360 365

ttt gat tgg tac aaa gct gtc agt ggg cta tat aca ata gat gtt gtt 1152  
Phe Asp Trp Tyr Lys Ala Val Ser Gly Leu Tyr Thr Ile Asp Val Val  
370 375 380

act gaa gaa aga agt gaa gaa gtt aaa aat gtt gaa tag 1191  
Thr Glu Glu Arg Ser Glu Glu Val Lys Asn Val Glu  
385 390 395

&lt;210&gt; 29

&lt;211&gt; 396

&lt;212&gt; PRT

&lt;213&gt; group B streptococcus

&lt;400&gt; 29

Val Asn Glu Ser Thr Ile Arg Lys Glu Phe Lys Ile Val Val Phe Lys  
1 5 10 15

Trp Ile Leu Asn Asn Gln Ala Val Ile Ala Leu Met Ile Thr Phe Leu  
20 25 30

Val Phe Leu Thr Ile Phe Ile Phe Thr Lys Ile Ser Phe Met Phe Lys  
35 40 45

Pro Val Phe Asp Phe Leu Ala Val Leu Ile Leu Pro Leu Val Ile Ser  
50 55 60

Gly Leu Leu Tyr Tyr Leu Leu Lys Pro Met Val Thr Phe Leu Glu Lys  
 65 70 75 80

Arg Gly Ile Lys Arg Val Thr Ala Ile Leu Ser Val Phe Thr Ile Ile  
 85 90 95

Ile Leu Leu Leu Ile Trp Ala Met Ser Ser Phe Ile Pro Met Met Ser  
 100 105 110

Asn Gln Leu Arg His Phe Met Glu Asp Leu Pro Ser Tyr Val Asn Lys  
 115 120 125

Val Gln Met Glu Thr Ser Ser Phe Ile Asp His Asn Pro Trp Leu Lys  
 130 135 140

Ser Tyr Lys Gly Glu Ile Ser Ser Met Leu Ser Asn Ile Ser Ser Gln  
 145 150 155 160

Ala Val Ser Tyr Ala Glu Lys Phe Ser Lys Asn Val Leu Asp Trp Ala  
 165 170 175

Gly Asn Leu Ala Ser Thr Val Ala Arg Val Thr Val Ala Thr Ile Met  
 180 185 190

Ala Pro Phe Ile Leu Phe Tyr Leu Leu Arg Asp Ser Arg Asn Met Lys  
 195 200 205

Asn Gly Phe Leu Met Val Leu Pro Thr Lys Leu Arg Gln Pro Ala Asp  
 210 215 220

Arg Ile Leu Arg Glu Met Asn Ser Gln Met Ser Gly Tyr Val Gln Gly  
 225 230 235 240

Gln Ile Ile Val Ala Ile Thr Val Gly Val Ile Phe Ser Ile Met Tyr  
 245 250 255

Ser Ile Ile Gly Leu Arg Tyr Gly Val Thr Leu Gly Ile Ile Ala Gly  
 260 265 270

Val Leu Asn Met Val Pro Tyr Leu Gly Ser Phe Val Ala Gln Ile Pro  
 275 280 285

Val Phe Ile Leu Ala Leu Val Ala Gly Pro Val Met Val Val Lys Val  
 290 295 300

Ala Ile Val Phe Val Ile Glu Gln Thr Leu Glu Gly Arg Phe Val Ser  
 305 310 315 320

Pro Leu Val Leu Gly Asn Lys Leu Ser Ile His Pro Ile Thr Ile Met  
325 330 335

Phe Ile Leu Leu Thr Ser Gly Ala Met Phe Gly Val Trp Gly Val Phe  
340 345 350

Leu Ser Ile Pro Ile Tyr Ala Ser Ile Lys Val Val Val Lys Glu Leu  
355 360 365

Phe Asp Trp Tyr Lys Ala Val Ser Gly Leu Tyr Thr Ile Asp Val Val  
370 375 380

Thr Glu Glu Arg Ser Glu Glu Val Lys Asn Val Glu  
385                      390                      395

<210> 30

<211> 1230

**<212> DNA**

<213> group B streptococcus

**<220>**

<221> CDS

<222> (1) .. (1230)

<400> 30

atg ttt atg gga atc cca caa tat ttc ttc tac ctt atc tta gct gtc 48  
Met Phe Met Gly Ile Pro Gln Tyr Phe Phe Tyr Leu Ile Leu Ala Val  
1 5 10 15

cta cca att tac atc ggc tta ttc ttt aag aag cgt ttt gcc tta tat 96  
Leu Pro Ile Tyr Ile Gly Leu Phe Phe Lys Lys Arg Phe Ala Leu Tyr  
20 25 30

gag att att ttt agt cta agt ttt att gta atg atg ttg act ggt agt 144  
Glu Ile Ile Phe Ser Leu Ser Phe Ile Val Met Met Leu Thr Gly Ser  
35 40 45

act ttt aat caa ttg aag tca cta ttg gca tac gtt gtc gga cag tct 192  
Thr Phe Asn Gln Leu Lys Ser Leu Leu Ala Tyr Val Val Gly Gln Ser  
50 55 60

ctg cta gtt ttt atc tat aaa gct tac cgg aaa cga ttt aat cat act 240  
Leu Leu Val Phe Ile Tyr Lys Ala Tyr Arg Lys Arg Phe Asn His Thr  
65 70 75 80

ttg qtc ttt tat gta acg gtt tgt tta tct att ttt ccg cta ttt ttg 288



Leu Val Phe Tyr Val Thr Val Cys Leu Ser Ile Phe Pro Leu Phe Leu	
85 90 95	
gta aaa tta att cca gct ata tct gag gat ggg cat cag tca ctt ttt	336
Val Lys Leu Ile Pro Ala Ile Ser Glu Asp Gly His Gln Ser Leu Phe	
100 105 110	
ggg ttt cta gga att tct tac ctt act ttt aga gct gtt gct atg att	384
Gly Phe Leu Gly Ile Ser Tyr Leu Thr Phe Arg Ala Val Ala Met Ile	
115 120 125	
att gaa atg aga gac ggt gtc ttg aaa gaa ttt act tta tgg gaa ttc	432
Ile Glu Met Arg Asp Gly Val Leu Lys Glu Phe Thr Leu Trp Glu Phe	
130 135 140	
tta aga ttt tta ctc ttc ttt cca act ttc tca agt gga cca att gat	480
Leu Arg Phe Leu Leu Phe Phe Pro Thr Phe Ser Ser Gly Pro Ile Asp	
145 150 155 160	
cgt ttt aaa cga ttc aat gag gat tac att aat atc cca gat cga aac	528
Arg Phe Lys Arg Phe Asn Glu Asp Tyr Ile Asn Ile Pro Asp Arg Asn	
165 170 175	
gaa ctc cta gat atg tta ggt caa gcg att cat tat ttg atg tta ggt	576
Glu Leu Leu Asp Met Leu Gly Gln Ala Ile His Tyr Leu Met Leu Gly	
180 185 190	
ttt ctc tat aag ttt att tta gcc tat att ttt gga agt ctg att atg	624
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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>7</sup> : <b>C12N 15/31, 15/57, 15/53, 15/56, 15/61, 1/21, A61K 39/09, C12Q 1/37, 1/32, 1/34, 1/533, G01N 33/68, C07K 16/12, A61K 48/00</b>		<b>A3</b>	(11) International Publication Number: <b>WO 00/37646</b> (43) International Publication Date: <b>29 June 2000 (29.06.00)</b>																																																			
(21) International Application Number: <b>PCT/GB99/04377</b> (22) International Filing Date: <b>22 December 1999 (22.12.99)</b>		(71) Applicant (for all designated States except US): <b>MICRO-SCIENCE LIMITED [GB/GB]; 545 Eskdale Road, Winkers Triangle, Wokingham, Berkshire RG41 5TU (GB).</b>																																																				
(30) Priority Data:		(72) Inventors; and (75) Inventors/Applicants (for US only): <b>HUGHES, Martin, John, Glenton [GB/GB]; Dept. of Infectious Diseases, Imperial College School of Medicine at the Hammersmith Campus, Du Cane Road, London W12 0NN (GB). SANTANGELO, Joseph, David [GB/GB]; Dept. of Infectious Diseases, Imperial College School of Medicine at the Hammersmith Campus, Du Cane Road, London W12 0NN (GB). LANE, Jonathan, Douglas [GB/GB]; Dept. of Infectious Diseases, Imperial College School of Medicine at the Hammersmith Campus, Du Cane Road, London W12 0NN (GB). EVEREST, Paul [GB/GB]; Dept. of Infectious Diseases, Imperial College School of Medicine at the Hammersmith Campus, Du Cane Road, London W12 0NN (GB). FELDMAN, Robert [GB/GB]; Dept. of Infectious Diseases, Imperial College School of Medicine at the Hammersmith Campus, Du Cane Road, London W12 0NN (GB). MOORE, Joanne, Christine [GB/GB]; Dept. of Infectious Diseases, Imperial College School of Medicine at the Hammersmith Campus, Du Cane Road, London W12 0NN (GB). WILSON, Rebecca, Kerry [GB/GB]; ICSTM, Dept. of Biochemistry, Exhibition Road, London SW7 2AZ (GB). DOBSON, Richard, James [GB/GB]; Dept. of Infectious Diseases, Imperial College School of Medicine at the Hammersmith Campus, Du Cane Road, London W12 0NN (GB). DOUGAN, Gordon [GB/GB]; ICSTM, Dept. of Biochemistry, Exhibition Road, London SW7 2AZ (GB).</b>																																																				
<table border="0"> <tr><td>9828359.1</td><td>22 December 1998 (22.12.98)</td><td>GB</td></tr> <tr><td>9828353.4</td><td>22 December 1998 (22.12.98)</td><td>GB</td></tr> <tr><td>9828352.6</td><td>22 December 1998 (22.12.98)</td><td>GB</td></tr> <tr><td>9828355.9</td><td>22 December 1998 (22.12.98)</td><td>GB</td></tr> <tr><td>9828354.2</td><td>22 December 1998 (22.12.98)</td><td>GB</td></tr> <tr><td>9828349.2</td><td>22 December 1998 (22.12.98)</td><td>GB</td></tr> <tr><td>9828345.0</td><td>22 December 1998 (22.12.98)</td><td>GB</td></tr> <tr><td>9828350.0</td><td>22 December 1998 (22.12.98)</td><td>GB</td></tr> <tr><td>9828357.5</td><td>22 December 1998 (22.12.98)</td><td>GB</td></tr> <tr><td>9828356.7</td><td>22 December 1998 (22.12.98)</td><td>GB</td></tr> <tr><td>9900084.6</td><td>4 January 1999 (04.01.99)</td><td>GB</td></tr> <tr><td>9900082.0</td><td>4 January 1999 (04.01.99)</td><td>GB</td></tr> <tr><td>9900085.3</td><td>4 January 1999 (04.01.99)</td><td>GB</td></tr> <tr><td>9900086.1</td><td>4 January 1999 (04.01.99)</td><td>GB</td></tr> <tr><td>9900083.8</td><td>4 January 1999 (04.01.99)</td><td>GB</td></tr> <tr><td>9901916.8</td><td>28 January 1999 (28.01.99)</td><td>GB</td></tr> <tr><td>9901922.6</td><td>28 January 1999 (28.01.99)</td><td>GB</td></tr> </table>		9828359.1	22 December 1998 (22.12.98)	GB	9828353.4	22 December 1998 (22.12.98)	GB	9828352.6	22 December 1998 (22.12.98)	GB	9828355.9	22 December 1998 (22.12.98)	GB	9828354.2	22 December 1998 (22.12.98)	GB	9828349.2	22 December 1998 (22.12.98)	GB	9828345.0	22 December 1998 (22.12.98)	GB	9828350.0	22 December 1998 (22.12.98)	GB	9828357.5	22 December 1998 (22.12.98)	GB	9828356.7	22 December 1998 (22.12.98)	GB	9900084.6	4 January 1999 (04.01.99)	GB	9900082.0	4 January 1999 (04.01.99)	GB	9900085.3	4 January 1999 (04.01.99)	GB	9900086.1	4 January 1999 (04.01.99)	GB	9900083.8	4 January 1999 (04.01.99)	GB	9901916.8	28 January 1999 (28.01.99)	GB	9901922.6	28 January 1999 (28.01.99)	GB	(74) Agent: <b>GILL JENNINGS &amp; EVERY; Broadgate House, 7 Eldon Street, London EC2M 7LH (GB).</b>	
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		Published With international search report.																																																				
		(88) Date of publication of the international search report: 26 October 2000 (26.10.00)																																																				
(54) Title: <b>GROUP B STREPTOCOCCUS PROTEINS, AND THEIR USE</b>																																																						
(57) Abstract																																																						
According to the present invention, a series of genes are identified in Group B <i>Streptococcus</i> , the products of which may be associated with the outer surface of the organism. The genes, or functional fragments thereof, may be useful in the preparation of therapeutics, e.g. vaccines to immunise a patient against microbial infection.																																																						



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# INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/04377

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/31 C12N15/57 C12N15/53 C12N15/56 C12N15/61  
C12N1/21 A61K39/09 C12Q1/37 C12Q1/32 C12Q1/34  
C12Q1/533 G01N33/68 C07K16/12 A61K48/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EPO-Internal, STRAND

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	LARSSON CHARLOTTE ET AL: "Experimental vaccination against group B streptococcus, an encapsulated bacterium, with highly purified preparations of cell surface proteins rib and alpha." INFECTION AND IMMUNITY 1996, vol. 64, no. 9, 1996, pages 3518-3523, XP002135397 ISSN: 0019-9567 the whole document --- -/--	6-11

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Date of the actual completion of the international search

30 June 2000

Date of mailing of the international search report

13.07.00

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Authorized officer

Van der Schaal, C

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/GB 99/04377

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>WÄSTFELT M ET AL: "Identification of a family of streptococcal surface proteins with extremely repetitive structure" JOURNAL OF BIOLOGICAL CHEMISTRY., vol. 271, no. 31, 2 August 1996 (1996-08-02), pages 18892-18897, XP002135770 MD US the whole document</p>	6-11
X	<p>GIFFARD PHILIP M ET AL: "The ftf gene encoding the cell-bound fructosyltransferase of Streptococcus salivarius ATCC 25975 is preceded by an insertion sequence and followed by FUR1 and clpP homologues." JOURNAL OF GENERAL MICROBIOLOGY 1993, vol. 139, no. 5, 1993, pages 913-920, XP000891932 ISSN: 0022-1287 cited in the application the whole document -&amp; EMBL DATABASE Accession no P36398 Sequence ID CLPP_STRSL 01 June 1994 XP002135400</p>	1-5,12
A	<p>MAURIZI M ET AL: "Sequence and structure of ClpP protease of Escherichia coli" JOURNAL OF BIOLOGICAL CHEMISTRY., vol. 265, no. 21, 25 July 1990 (1990-07-25), pages 12536-12545, XP002135771 MD US</p>	
E	<p>WO 00 06736 A (HANNIFFY SEAN BOSCO ;LE PAGE RICHARD WILLIAM FALLA (GB); WELLS JER) 10 February 2000 (2000-02-10) the whole document especially SEQ ID NO 27 and 28</p>	1-12
X	<p>TSUKIOKA YUICHI ET AL: "Biological function of the dTDP-Rhamnose synthesis pathway in Streptococcus mutans." JOURNAL OF BACTERIOLOGY, vol. 179, no. 4, 1997, pages 1126-1134, XP002141323 ISSN: 0021-9193 the whole document -&amp; EMBL DATABASE Accession no P95779 Sequence ID P95779 1 May 1997 XP002141324</p>	1-5,12

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# INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/04377

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>EMBL DATABASE Accession no 054547 Sequence  ID 054547  1 June 1998  COFFEY T ET AL: "Recombinational exchanges  at the capsular polysaccharide  biosynthesis locus...."  XP002141325  the whole document  &amp; MOLECULAR MICROBIOLOGY,  vol. 27, 1998, pages 73-83,  -----</p>	1-5,12

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/GB 99/04377

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
  
Although claim 7 is partially directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:  
  
1-12 invention 1, 6, 8, 9, and 10
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-12 partially

Pho1-13, nucleotides encoding the protein, antibody against the protein and their uses

2. Claims: 1-12 partially

Pho3-21, nucleotides encoding the protein, antibody against the protein and their uses

3. Claims: 1-12 partially

Pho2-15, nucleotides encoding the protein, antibody against the protein and their uses

4. Claims: 1-12 partially

Pho3-18, nucleotides encoding the protein, antibody against the protein and their uses

5. Claims: 1-12 partially

Pho3-22, nucleotides encoding the protein, antibody against the protein and their uses

6. Claims: 1-12 partially

Pho3-3, nucleotides encoding the protein, antibody against the protein and their uses

7. Claims: 1-12 partially

Pho3-17, nucleotides encoding the protein, antibody against the protein and their uses

8. Claims: 1-12 partially

Pho2-2, nucleotides encoding the protein, antibody against the protein and their uses

9. Claims: 1-12 partially

Pho1-5, nucleotides encoding the protein, antibody against the protein and their uses

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

10. Claims: 1-12 partially

Pho3-1, nucleotides encoding the protein, antibody against the protein and their uses

11. Claims: 1-12 partially

Pho3-23, nucleotides encoding the protein, antibody against the protein and their uses

12. Claims: 1-12 partially

Pho3-50, nucleotides encoding the protein, antibody against the protein and their uses

13. Claims: 1-12 partially

Pho1-14, nucleotides encoding the protein, antibody against the protein and their uses

14. Claims: 1-12 partially

Pho2-10, nucleotides encoding the protein, antibody against the protein and their uses

15. Claims: 1-12 partially

Pho3-14, nucleotides encoding the protein, antibody against the protein and their uses

16. Claims: 1-12 partially

Pho3-24, nucleotides encoding the protein, antibody against the protein and their uses

17. Claims: 1-12 partially

Pho3-29, nucleotides encoding the protein, antibody against the protein and their uses

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 99/04377

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0006736 A	10-02-2000	NONE	